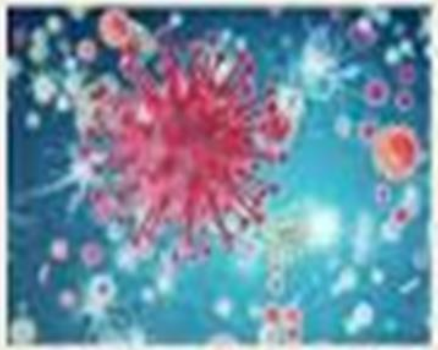

Management of HIV in pregnancy and Interventions to Reduce Perinatal HIV Transmission

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Introduction

- CDC has developed a goal of eliminating perinatal HIV transmission in the United States, defined as reducing perinatal transmission to an incidence of <1 infection per 100,000 live births and to a rate of <1% among infants exposed to HIV.

- However, incomplete implementation of routine antenatal HIV testing and other recommended interventions remains a barrier to achieving this goal.

Introduction

- Every year, approximately 5,000 women with HIV give birth in the United States.
- In addition to primary prevention of HIV infection in people who can become pregnant, the best way to prevent HIV infection in infants is to focus on appropriate overall medical care for women, with HIV.
- A critical component of preventing perinatal HIV transmission is ensuring that a pregnant person with HIV receives ART that sustainably suppresses viral replication to below the level of viral load assay detection as early as possible during pregnancy or, ideally, before conception.

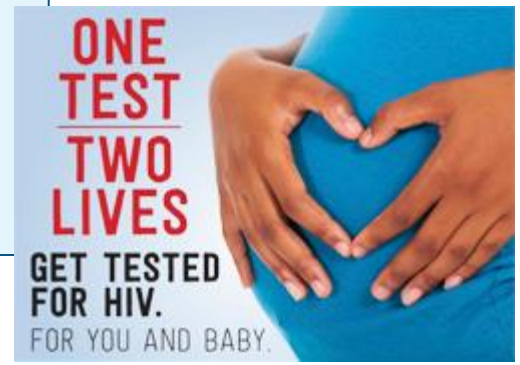
Introduction

- **Selection of ARV drugs should be individualized according to the pregnant person's ARV history, results of drug-resistance testing, and presence of comorbidities.**

- **In general, people who are already on a fully suppressive regimen when pregnancy occurs should continue their regimens.**

Maternal HIV Testing and Identification of Perinatal HIV Exposure

- HIV infection should be identified before pregnancy or as early as possible in pregnancy.
- HIV testing is recommended as a standard of care for all sexually active people and should be a routine component of pre pregnancy care.
- All pregnant people should be tested as early as possible during each pregnancy.
- Partners of all pregnant people should be referred for HIV testing when their status is unknown.



Repeat HIV Testing in the Third Trimester (before 36 weeks gestation)

- ***Who are at high risk of acquiring HIV :***
- those who inject drugs or have sex with people who inject drugs,
- those who exchange sex for money or drugs,
- those who have a sex partner with HIV who has a detectable or unknown HIV viral load
- those who have had a new sex partner or more than one sex partner during the current pregnancy

- those who have a suspected or diagnosed STI during pregnancy
- ***Have signs or symptoms of acute HIV***
- those who have recently immigrated from a high-burden HIV setting, or those who have a partner who either recently immigrated from a high-burden HIV setting or recently traveled to such a setting)

Maternal HIV Testing and Identification of Perinatal HIV Exposure

Expedited HIV testing should be performed during labor or delivery for people with undocumented HIV status and for those who tested negative early in pregnancy but are at increased risk of HIV infection and were not retested in the third trimester.

Prepregnancy Counseling and Care for Persons of Childbearing Age with HIV

- Discuss reproductive desires with all persons of childbearing potential on an ongoing basis throughout the course of their care.
- Provide information about effective and appropriate contraceptive methods to people who do not currently desire pregnancy.
- During prepregnancy counseling, provide information on safe sex; ask about the use of alcohol, nicotine products, and drugs of abuse.

Prepregnancy Counseling and Care for Persons of Childbearing Age with HIV

- Persons with HIV should attain maximum viral suppression before attempting conception, for their own health, to prevent sexual HIV transmission to partners without HIV , and to minimize the risk of in utero HIV transmission to the infant.

- When fully suppressive ART is started before pregnancy and undetectable viral load is maintained throughout pregnancy and at delivery, the risk of HIV transmission to the infant is extremely low (<1%).

Prepregnancy Counseling and Care for Persons of Childbearing Age with HIV

When selecting or evaluating an ARV regimen for people of childbearing potential with HIV, consider a regimen's effectiveness, **changes in ARV pharmacokinetics in the second and third trimesters of pregnancy,** a person's hepatitis B status, and the possible adverse outcomes for the pregnant person and their fetus.

HIV infection does not preclude the use of any contraceptive method; however, drug-drug interactions between hormonal contraceptives, ARVs, and other medications should be considered.

Evaluate and manage ART-associated adverse effects (e.g., hyperglycemia, anemia,hepatotoxicity) that may affect health outcomes for the pregnant person and fetus.

Administer **all vaccines** as indicated which includes vaccination for influenza, pneumococcus, HBV, tetanus, and SARS-CoV-2. All people, including those with HIV, should receive **Tdap** (tetanus, diphtheria, and pertussis) vaccination during each pregnancy typically between 27 and 36 weeks of gestation but preferably as early in this time window as possible.

Reproductive Options Both Partners Have HIV

- **Considerations When Both Partners Have HIV:**

- People with HIV should achieve **sustained viral suppression** (**e.g., two recorded measurements of plasma viral loads that are below the limits of detection at least 3 months apart**) before attempting conception to maximize their health, prevent HIV sexual transmission.

- **Both persons should be screened and treated for genital tract infections before attempting to conceive.**

Reproductive Options When One Partners Have HIV

- **When partners with different HIV statuses attempt conception:**
- **Before trying to pregnancy, a person with HIV should undergo ART and have a sustained undetectable viral load .**
- **When a woman is infected with HIV and her partner is not:**
- After the start of treatment and a sustained undetectable viral load,then the best way to have a child is **Intra uterine artificial insemination.**

Reproductive Options When One Partners Have HIV

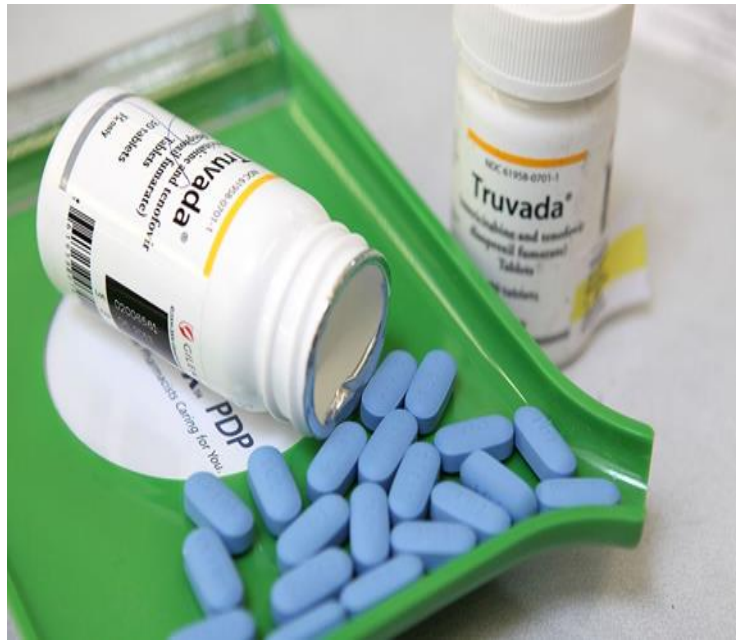
- When partners with different HIV statuses attempt conception, the partner without HIV can choose to take **PrEP.**

- **PrEP for the person without HIV is an option that reduces the risk of sexual acquisition of HIV when:**
- **The person with HIV has not achieved sustained viral suppression or their HIV viral suppression status is unknown.**
- **Concerns exist that the person with HIV might be inconsistently adherent to ART during the periconception period.**

Pre-exposure Prophylaxis (PrEP) to Prevent HIV During Periconception And Antepartum

- **Daily oral combination (TDF/FTC)** pre-exposure prophylaxis (PrEP), when indicated, for uninfected individuals who are trying to conceive or are pregnant, to prevent HIV acquisition.

- Indications for PrEP include risk factors for acquiring HIV, such **as condomless sex with a partner with HIV whose HIV-RNA level is detectable or unknown**, **recent STI,** or **injection drug use.**



Pre-exposure Prophylaxis (PrEP) to Prevent HIV During Periconception And Antepartum

Tenofovir alafenamide (TAF)/FTC has not yet been studied for efficacy in people with vaginal exposure;therefore, TAF/FTC is not recommended for this population, including during pregnancy and postpartum.

Pre-exposure Prophylaxis (PrEP) to Prevent HIV During Periconception And Antepartum

- Providers should offer routine PrEP follow-up, including **testing for HIV every 3 months** and counseling on signs and symptoms of acute retroviral syndrome.
- Renal function testing is recommended at baseline and then every 12 months for persons <50 years of age and/or with estimated CrCl over 90 mL/min.
- Otherwise,renal function should be monitored every 6 months.
- TDF/FTC as PrEP should not be initiated in patients with a confirmed calculated CrCl <60 mL/min.
- Clinicians should discontinue daily TDF/FTC as PrEP if a patient develops a confirmed calculated CrCl <50 mL/min.

Pregnancy testing should be completed at baseline and then every 3 months for those who can become pregnant.

Time to Protection

Studies in nonpregnant women demonstrate that it may take up to 20 days to reach maximum intracellular concentrations of tenofovir and/or FTC in cervicovaginal tissue, compared to only 7 days in anal tissues.

the Panel recommends continued use of other prevention strategies until PrEP has been taken for at least 20 days and protection against transmission can be assumed in pregnant or postpartum PrEP users.

When people initiate PrEP and have not yet reached protective drug levels or struggle with daily adherence, other strategies (e.g., condoms)should be used to prevent HIV.

Time to Protection

- **Therefore, the Panel recommends 20 days of PrEP before considering an individual fully protected from HIV acquisition via vaginal exposure.**

- **For people planning to discontinue daily oral PrEP, ongoing use for 7 to 28 days after last HIV exposure is recommended. This time frame aligns with recommendations for post-exposure Prophylaxis.**

Reproductive Options When One Partners Have HIV

- **3 weeks after the completion of PrEP in the pregnant mother, the fourth generation HIV ELISA test should be performed and then repeated 3 months later.**

Antepartum Care for Individuals With HIV

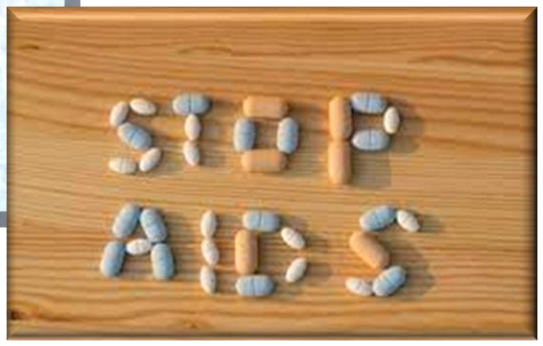
- In addition to the standard antepartum assessments for all pregnant people, the initial evaluation of people with HIV should include an assessment of HIV disease status and recommendations for HIV-related medical care.

Antepartum Screenings and Assessments for Pregnant People With HIV

Antepartum screenings and assessments	At Entry Into Antenatal Care	At Each Visit	As Clinically Indicated
Assessment of ART adherence, adherence challenges, and facilitators	✓	✓	✓
Assessment of the need for prophylaxis against opportunistic infections(e.g., Pneumocystis jirovecii Pneumonia)	✓		✓
Screening for HAV, HBV, and HCV and assessment of vaccination or treatment needs	✓		
Assessment and provision of other vaccination needs, e.g., influenza, pneumococcus, Tdap, or SARS-CoV-2 (including boosters)	✓		✓
STI screening, e.g., syphilis, *Chlamydia trachomatis*, *Trichomonas vaginalis*, and *Neisseria gonorrhea*	✓		✓
Screening for depression and anxiety	✓		✓
Assessment of the need for supportive care, e.g., social services, mental health services, substance use disorder treatment services, smoking cessation	✓	✓	✓

Antepartum Care for Individuals With HIV

- **Initial evaluation of pregnant people with HIV should include an assessment of HIV disease status and plans to initiate, continue, or modify antiretroviral therapy.**
- **All pregnant people with HIV should initiate ART as early in pregnancy as possible, regardless of their HIV RNA level or CD4 T lymphocyte count, to maximize their health and prevent perinatal HIV transmission .**
- If an ARV drug regimen must be stopped during pregnancy (e.g., for severe toxicity), all ARV drugs should be stopped simultaneously, and a complete, effective ARV regimen should be reinitiated as soon as possible.



Antepartum Care for Individuals With HIV

- The ideal ART regimen during pregnancy depends on multiple factors, including:
- **pharmacokinetics, virologic efficacy, safety, side effects, drug resistance, dosing convenience, local cost, and availability.**
- The main questions pertain to which ART regimens have the best safety and side-effect profiles when used during pregnancy.

- **ART regimens currently recommended during pregnancy include two nucleoside reverse-transcriptase inhibitors in combination with ART from a different class.**
- This review focuses on contemporary ART regimens but includes some data on “legacy” antiretroviral agents that are still used by many persons in low- and middle-income countries.

Table 1. Antiretroviral Therapy (ART) Regimens for Use in Pregnant Persons Living with Human Immunodeficiency Virus (HIV).*

Guideline	Nucleoside Reverse-Transcriptase Inhibitors	Nonnucleoside Reverse-Transcriptase Inhibitors	Integrase Strand-Transfer Inhibitors	Protease Inhibitors	Monoclonal Antibodies
Preferred or recommended antiretroviral agents					
WHO perinatal HIV guideline (2021)	TDF Emtricitabine Lamivudine	None	Dolutegravir	None	None
DHHS guideline (2023) **(2024)**	TAF Emtricitabine TDF Lamivudine Abacavir†	None	Dolutegravir	Darunavir–ritonavir (600 mg/100 mg twice daily)	None
EACS perinatal HIV guideline (2022)	TAF (after 14 wk of gestation) Emtricitabine TDF Lamivudine Abacavir†	None	Dolutegravir Raltegravir (400 mg twice daily)	Darunavir–ritonavir (600 mg/100 mg twice daily)	None

Alternative regimens					
WHO (2021)	None	Low-dose efavirenz (400 mg)	None	Atazanavir–ritonavir Darunavir–ritonavir Lopinavir–ritonavir	None
DHHS (2023) **(2024)**	Zidovudine	Efavirenz Oral rilpivirine	Raltegravir	Atazanavir–ritonavir	None
EACS (2022)	None	Efavirenz Oral rilpivirine	None	None	None
Not recommended					
DHHS (2023) **(2024)**	None	None	Elvitegravir–cobicistat	Darunavir–cobicistat Atazanavir–cobicistat Lopinavir–cobicistat	None

National guidelines of Iran

جدول شماره ۱ : رژیم درمان آغازین ضدترووویروسی در مادر باردار

Recommended Initial Regimens
INSTI + 2 NRTI regimen • DTG plus (TDF or TAF①) plus (FTC or 3TC) • DTG /ABC②/3TC
Alternative regimens
Boosted PI + 2 NRTI regimen • DRV/r④ plus (TDF or TAF) plus (FTC or 3TC) • ATV/r plus (TDF or TAF) plus (FTC or 3TC) • DRV/r plus ABC/3TC • **INSTI + 2 NRTI regimen** • RAL plus (TDF or TAF) plus (FTC or 3TC) **NNRTI + 2 NRTI regimen** • EFV⑤ 600 mg plus TDF plus (FTC or 3TC) • EFV 600 mg plus TAF/FTC

Situation-Specific Recommendations for Use of Antiretroviral Drugs in Pregnant People and Nonpregnant People Who Are Trying to Conceive

ART Regimen Component	ART for Pregnant People Who Have Never Received ARV Drugs and Who Are Initiating ART for the First Time	Continuing ART for People Who Become Pregnant on a Fully Suppressive, Well-Tolerated Regimen	ART for Pregnant People Who Have Received ARV Drugs in the Past and Who Are Starting or Restarting ART[a]	New ART Regimen for Pregnant People Whose Current Regimen Is Not Well Tolerated and/or Is Not Fully Suppressive	ART for Nonpregnant People Who Are Trying to Conceive[b]
Integrase Strand Transfer Inhibitor (INSTI) Drugs Used in combination with a dual–nucleoside reverse transcriptase inhibitor (NRTI) backbone[c,d]					
DTG[a]	Preferred[a]	Continue	Preferred[a]	Preferred	Preferred
BIC[a,e]	Alternative[a]	Continue	Alternative[a]	Alternative	Alternative
RAL	Alternative	Continue	Alternative	Alternative	Alternative
CAB[d] Oral (lead-in) Long-acting (IM)	Not recommended	Continue with frequent viral load monitoring or consider switching due to insufficient data[d]	Insufficient data	Insufficient data	Insufficient data

Updated: January 31, 2024
Reviewed: January 31, 2024

Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States

Antepartum Care for Individuals With HIV

Pregnant women with HIV who are currently receiving antiretroviral drugs :

- **They should continue their current ART, especially in cases where the drug is tolerated and the viral load is suppressed.**
- **If the viral load is not suppressed, it is recommended to use the drug-resistance testing.**

Adverse Fetal and Birth Outcomes

- With the exception of congenital anomalies, adverse birth outcomes (specifically fetal loss,preterm birth, intrauterine growth restriction,small for gestational age, and low birth weight) receive much less attention than prevention of HIV transmission, despite the large effect of these outcomes on the population.

- In the pre-ART era, persons living with HIV infection had worse birth outcomes than uninfected persons, including twice the rates of preterm birth, low birth weight, and stillbirth.

- **birth outcomes are better in pregnant persons with HIV who are receiving ART than in those not receiving ART.**

Congenital Anomalies

- **EFV and DTG** deserve special mention.
- Early nonhuman primate studies suggested the possibility of central nervous system malformations with EFV, but large cohort studies and antiretroviral pregnancy registries have **not shown this association in humans**.
- the prevalence of neural-tube defects with periconception DTG exposure declined and **is now similar to that in the general population.**

- **Based on the available evidence,DTG as a Preferred drug for pregnant people, irrespective of trimester , and for people who are trying to conceive.**
- **Folic acid is known to prevent NTDs. All pregnant people and people who might conceive should take at least 400 mcg of folic acid daily.**

Hypertensive Disorders of Pregnancy

- ART has **not been associated** with an increased risk of hypertensive disorders of pregnancy (gestational hypertension, chronic hypertension,HELLP [hemolysis, elevated liver-enzyme levels,and a low platelet count] syndrome, and preeclampsia)in most studies.

- **There is currently insufficient evidence to recommend preventive therapies (e.g., low-dose aspirin) to mitigate the risk of preeclampsia in pregnant persons living with HIV who are receiving ART and do not have other known risk factors for preeclampsia.**

Peripartum Depression

- Some antiretroviral agents (e.g.,**EFV** and, less frequently, **rilpivirine** and **DTG**) have been associated with a risk of depression and suicidal thoughts in adults.

- **Screening for antepartum and postpartum depression is advised.**

Initial Evaluation and Continued Monitoring of HIV-Related Assessments During Pregnancy

- Viral Load
- HIV drug-resistance testing
- CD4 Count
- Laboratory testing to monitor complications of ARV drugs
- Ultrasound of the fetus
- standard glucose screening

Initial Evaluation and Continued Monitoring of HIV-Related Assessments During Pregnancy

- **CBC:** Performed at **ART initiation** or **entry into prenatal care,** at **28–36 wk of gestation**, and if anemia is suspected (especially with zidovudine-based regimen)

- **basic metabolic panel with liver function tests:**

  Performed **at ART initiation or entry into prenatal care** and **within 2–4 wk after initiating or changing ART,** with **checks every 3 months afterward or as needed**

- **Glucose screening for diabetes:**

  Performed in **first or early third trimester** or both

“Intrapartum Care” for People with HIV

- **HIV Testing for Pregnant People with Unknown HIV Status in Labor:**
- Pregnant people who present in labor with unknown HIV status and people with increased risk of HIV infection who were not retested in the third trimester should undergo expedited **antigen/antibody HIV testing.**
- **If results are positive, an HIV-1/HIV-2 antibody should be done as soon as possible, and (IV) zidovudine (ZDV) should be initiated pending the result of the differentiation test.**
- **2 mg /kg of the mother's weight was infused during the first hour, and then it continued as a continuous infusion of zidovudine at the rate of 1 mg /kg of the mother's weight per hour until delivery.**

“Intrapartum Care” for People with HIV

- **Intrapartum Antiretroviral Therapy ,ZDV Prophylaxis, and Mode of Delivery for Pregnant People with HIV:**

HIV RNA at Time of Delivery Assessed at 36 Weeks Gestation or Within 4 Weeks of Delivery with No Concerns Regarding ART Adherence[a]				
	<50 copies/mL and on ART with No Concerns About Adherence	**≥50 to ≤1,000 copies/mL**	**>1,000 copies/mL**	**Unknown HIV RNA ART Adherence Concerns Not Receiving ART HIV Diagnosis in Labor**
Intrapartum ART	Pregnant people should take their prescribed ART on schedule as much as possible during labor and before scheduled cesarean delivery **(CIII).** In general, ARV regimens are initiated postpartum for people diagnosed with HIV during labor.			
Intrapartum IV ZDV	Not required **(BII).**	Not required but may be considered **(CII)**; many experts recommend.	Yes, recommended **(AI).**[b] IV ZDV: 1-hour loading dose at 2 mg/kg followed by a continuous ZDV infusion of 1 mg/kg for 2 hours (at least 3 hours total) **(AII).**	
Mode of delivery	Normal vaginal delivery[c] **(AII).**	Normal vaginal delivery[c] **(AII).**	Scheduled cesarean delivery at 38 weeks[d] **(AII).**	Individualized care, see footnote.[d]

“Intrapartum Care” for People with HIV

- Patients should continue taking their antepartum ART on schedule during labor and before scheduled cesarean delivery:
- ***Intrapartum IV ZDV:***
- **(a) HIV RNA >1,000 copies/mL,**
- **(b) unknown viral load,**
- **(c) known or suspected lack of adherence since the last HIV RNA result**
- **(d) a positive expedited antigen/antibody HIV test result during labor**

- **In pregnant people on ART with HIV RNA ≤1,000 copies/mL, duration of ruptured membranes is not associated with an increased risk of perinatal transmission and is not an indication for cesarean delivery to prevent HIV transmission.**

Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection

- All newborns who were exposed perinatally to HIV should receive postpartum ARV drugs to reduce the risk of perinatal transmission of HIV.
- Newborn ARV regimens administered at doses that are appropriate for the infant's gestational age should be initiated as close to the time of birth as possible, preferably **within 6 hours of delivery.**
- ***ARV Prophylaxis:*** The administration of one or more ARV drugs to a newborn without documented HIV infection to reduce the risk of perinatal acquisition of HIV.

Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection

For newborns at low-risk of perinatal HIV acquisition, a 2-week zidovudine (ZDV) ARV regimen is recommended for ARV prophylaxis if the newborn is ≥37 weeks gestation and is born to a person with HIV who:

- Is currently receiving and has received at least 10 consecutive weeks of ART during pregnancy and
- Has achieved and maintained or maintained viral suppression (defined as at least two consecutive tests with HIV RNA <50 copies/mL obtained at least 4 weeks apart) for the duration of pregnancy ; and
- Has a viral load <50 copies/mL at or after 36 weeks ; and
- Did not have acute HIV infection during pregnancy and
- Has reported good ART adherence, and adherence concerns have not been identified.

Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection

Infants born to individuals who do not meet the criteria above but who have a viral load <50 copies/mL at or after 36 weeks gestation should receive ZDV for 4 to 6 weeks.

All premature infants <37 weeks gestation who are not at high risk of perinatal acquisition of HIV should receive ZDV for 4 to 6 weeks.

Newborns at high risk of perinatal acquisition of HIV should receive presumptive HIV therapy with 3-drug regimens administered from birth for 2 to 6 weeks , if the duration of the 3-drug regimen is shorter than 6 weeks, ZDV should be continued alone, to complete total of 6 weeks of prophylaxis.

Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection

- Have not received antepartum ARV drugs , or
- Have received only intrapartum ARV drugs, or
- Have received antepartum ARV drugs but who did not achieve viral suppression (defined as at least two consecutivetests with HIV RNA level <50 copies/mL obtained at least 4 weeks apart) within 4 weeks of delivery) or
- Have primary or acute HIV infection during pregnancy

Newborns at high risk of HIV acquisition include those born to people with HIV who

Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection

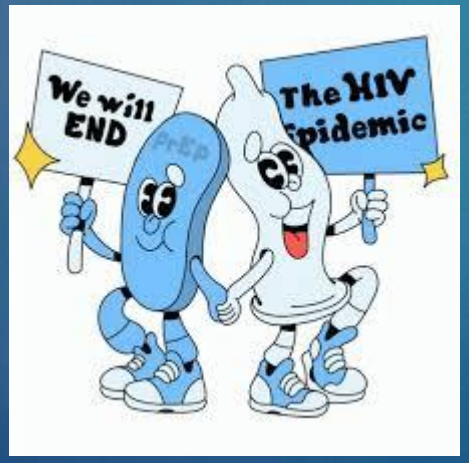
Presumptive HIV therapy: using either ZDV, 3TC, and NVP (treatment dose) or ZDV, 3TC, and RAL administered together .

Newborns at high risk of HIV acquisition include those born to people with HIV who

Initial Postnatal Management of the Neonate Exposed to HIV

- ARV drugs as soon as possible.
- Nucleic acid tests (i.e. DNA and RNA PCR, RNA PCR assays) are required to diagnose HIV infection in infants aged <18 months.
- To prevent Pneumocystis jirovecii pneumonia (PJP), all infants born to persons with HIV should begin PJP prophylaxis at age 4 to 6 weeks, unless adequate test information is available to presumptively exclude HIV infection.


THANK YOU


We will END
The HIV Epidemic