

## Intrapartum Care for Women with HIV

(Last updated December 29, 2020; last reviewed December 29, 2020)

### Panel's Recommendations

#### HIV Testing for Women with Unknown HIV Status in Labor

- Women who present in labor with unknown HIV status and women with increased risk of HIV infection who were not retested in the third trimester should undergo expedited antigen/antibody HIV testing (AII). See [Maternal HIV Testing and Identification of Perinatal HIV Exposure for more information](#).
  - If results are positive, an HIV-1/HIV-2 antibody differentiation test and an HIV-1 RNA assay should be done as soon as possible, and intravenous (IV) zidovudine (ZDV) should be initiated pending the result of the differentiation test (AII).
  - If acute HIV infection is suspected or if a woman has had recent HIV exposure, an HIV RNA assay should be done at the time of expedited antigen/antibody testing (AII). See [Acute HIV Infection](#).

#### Intrapartum Antiretroviral Therapy (ART), Zidovudine (ZDV) Prophylaxis, and Mode of Delivery for Women with HIV

- See [Table 7 Intrapartum Care and Recommended Interventions to Prevent Perinatal HIV Transmission for Women with HIV based on Maternal HIV RNA Levels at the Time of Delivery](#) below.
- Women should continue taking their antepartum ART on schedule, during labor and before scheduled cesarean delivery (AIII).
- **For women with HIV RNA >1,000 copies/mL or unknown HIV RNA near the time of delivery (≥34 to 36 weeks gestation or 4 to 6 weeks before delivery):**
  - Intrapartum IV ZDV should be administered in the following situations based on laboratory and clinical information near the time of delivery: (a) HIV RNA >1,000 copies/mL, (b) unknown HIV RNA, (c) a suspected lack of adherence since the last HIV RNA result, or (d) a positive expedited antigen/antibody HIV test result during labor (AI). Begin IV ZDV when women present in labor or at least 3 hours prior to scheduled cesarean delivery (AII).
  - When HIV RNA is >1,000 copies/mL or is unknown near the time of delivery, scheduled cesarean delivery at 38 weeks gestation is recommended to minimize perinatal HIV transmission, irrespective of administration of antepartum ART (AII).
  - Management of women originally scheduled for cesarean delivery because of HIV RNA >1,000 copies/mL who present in labor or with ruptured membranes must be individualized at the time of presentation (BII). In these circumstances, evidence is insufficient to determine whether cesarean delivery reduces the risk of perinatal HIV transmission. Consultation with an expert in perinatal HIV (e.g., telephone consultation with the National Perinatal HIV/AIDS Clinical Consultation Center at 1-888-448-8765) may be helpful in rapidly developing an individualized delivery plan.
- **For women receiving ART with HIV RNA ≤1,000 copies/mL near the time of delivery (≥34 to 36 weeks gestation or 4 to 6 weeks before delivery):**
  - IV ZDV is not required for women who meet **ALL** of the following three criteria: (1) are receiving ART, (2) have HIV RNA <50 copies/mL at ≥34 to 36 weeks gestation (or 4–6 weeks before delivery), and (3) are adherent to their antiretroviral (ARV) regimen (BII).
  - IV ZDV may be considered for women with HIV RNA ≥50 copies/mL and ≤1,000 copies/mL near delivery (≥34 to 36 weeks gestation) (BII). Data are insufficient to determine whether administration of IV ZDV to women with HIV RNA levels between 50 copies/mL and 1,000 copies/mL provides any additional protection against perinatal HIV transmission. This decision can be made on a case-by-case basis, taking into consideration the woman's recent ART adherence and her preferences and involving expert consultation if needed (CII).
  - Scheduled cesarean delivery performed solely for prevention of perinatal HIV transmission in women receiving ART with HIV RNA ≤1,000 copies/mL near the time of delivery **is not recommended** given the low rate of perinatal transmission in this group (AII).
  - In women with HIV RNA levels ≤1,000 copies/mL, if scheduled cesarean delivery or induction of labor is indicated for non-HIV-related reasons, it should be performed at the standard time for obstetric indications (AII). Labor should not be induced to prevent perinatal HIV transmission.

- In women on ART with HIV RNA  $\leq 1,000$  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 (BII).

#### Other Intrapartum Management Considerations (see [Table 7](#) below).

- Fetal scalp electrodes for fetal monitoring should be avoided, particularly when maternal HIV RNA is not suppressed ( $\geq 50$  copies/mL) or is unknown, because of the potential risk of HIV transmission (BIII). See [Antiretroviral Management of Newborns with Perinatal HIV Exposure or Perinatal HIV](#).
- Artificial rupture of membranes (ROM) and operative vaginal delivery with forceps or a vacuum extractor should follow standard obstetric indications but should be avoided if possible in women with HIV RNA  $\geq 50$  copies/mL (BIII).
- The ARV regimen a woman is receiving should be taken into consideration when using methergine to treat excessive postpartum bleeding caused by uterine atony.
  - In women who are receiving a cytochrome P450 (CYP) 3A4 enzyme inhibitor (e.g., a protease inhibitor or cobicistat), methergine should be used only if no alternative treatments for postpartum hemorrhage are available and the need for pharmacologic treatment outweighs the risks. If methergine is used, it should be administered at the lowest effective dose for the shortest possible duration (BIII).
  - In women who are receiving a CYP3A4 enzyme inducer—such as nevirapine, efavirenz, or etravirine—additional uterotonic agents may be needed because of the potential for decreased methergine levels and inadequate treatment effect (BIII).

**Rating of Recommendations:** A = Strong; B = Moderate; C = Optional

**Rating of Evidence:** I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

### Overview of Intrapartum Care for Women with HIV

Women with HIV require specialized care during labor and delivery to optimize maternal health outcomes and to prevent perinatal HIV transmission. Documentation of HIV status should be assessed in all women during labor, and HIV testing should be offered to those with unknown or undocumented HIV status, recent HIV exposure, and/or signs of acute HIV (see [Maternal Testing and Identification of Perinatal HIV Exposure and Acute HIV Infection](#)). Because maternal HIV RNA level is directly linked to the risk of perinatal HIV transmission,<sup>1</sup> the Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission (Panel) recommends viral load testing throughout pregnancy and specifically at 34 to 36 weeks gestation (or 4–6 weeks before delivery) to inform decisions about intrapartum care. The risk of perinatal HIV transmission is reduced to very low levels in pregnant women receiving antiretroviral therapy (ART) who have documented viral suppression ( $< 50$  copies/mL) near delivery.<sup>1–3</sup> Panel recommendations about intrapartum care to prevent HIV transmission are based on maternal HIV RNA levels and encompass continuation of maternal ART, intrapartum intravenous (IV) zidovudine (ZDV) during labor and delivery, scheduled cesarean delivery, and other intrapartum management considerations. Table 7 provides an overview of the Perinatal Panel recommendations for intrapartum care based on maternal HIV RNA, but these recommendations are discussed in the following sections.

### Women Who Present in Labor Without Documentation of HIV Status

All women without documentation of HIV status at the time of labor should be screened for HIV with expedited testing unless they decline (i.e., “opt-out” screening) (see [Maternal HIV Testing and Identification of Perinatal HIV Exposure](#)). Expedited repeat HIV testing is also recommended for women who present in labor and who tested negative for HIV in early pregnancy, but who are at increased risk of HIV infection and were not retested in the third trimester.<sup>4,5</sup> Factors that may increase the risk of infection include diagnosis of a sexually transmitted infection, illicit drug use, exchange of sex for money or drugs, multiple sexual partners during pregnancy, a

sexual partner who is at risk of HIV infection or who is known to have HIV, signs or symptoms of acute HIV infection, or living in a region with an elevated incidence of HIV in women of childbearing age.<sup>4</sup> Women who test positive on the initial HIV test during labor should be presumed to have HIV until follow-up testing clarifies their HIV status. To prevent perinatal HIV transmission, intrapartum IV ZDV should be started immediately, as discussed below, and women should not initiate breastfeeding until HIV infection is definitively ruled out. For additional information, see [Postpartum Follow-up of Women with HIV Infection and Care](#), [Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection](#), and [Table 9](#).

Initial testing for HIV should be done with a Food and Drug Administration (FDA)-approved antigen/antibody combination immunoassay that detects HIV-1 and HIV-2 antibodies. No further testing is required for specimens that are nonreactive on the initial immunoassay, unless the woman has had recent HIV exposure or acute infection is suspected, in which case, an HIV RNA assay should be obtained (see [Maternal HIV Testing and Identification of Perinatal HIV Exposure](#)). Women with an initial positive antigen/antibody combination immunoassay result should be tested with an FDA-approved antibody immunoassay that differentiates HIV-1 antibodies from HIV-2 antibodies and an HIV RNA assay to screen for both acute and chronic HIV-1 infection (see [Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings](#) and the resource page for [laboratory testing for HIV](#) from the Centers for Disease Control and Prevention). If the follow-up antibody test result is negative, results of the HIV RNA test should be reviewed to rule out acute infection as a cause of the initial positive test result before ART is stopped (see [Acute HIV Infection](#)). Those with a high level of HIV-1 RNA and a negative confirmatory HIV assay most likely have acute HIV infection. If both the HIV-1 RNA and the confirmatory HIV assay are negative, the initial HIV test result may have been a false positive.

Expedited HIV testing should be available on a 24-hour basis at all facilities with a maternity service and/or neonatal intensive care unit. Statutes and regulations regarding expedited testing vary from state to state (see [State HIV Testing Laws](#) from the Clinician Consultation Center and [State Laws That Address High-Impact HIV Prevention Efforts](#)).

### **Intrapartum Continuation of Antenatal Antiretroviral Drugs**

ART is recommended for the treatment of HIV and prevention of perinatal HIV transmission in all pregnant women with HIV, regardless of CD4 T lymphocyte (CD4) cell count and HIV RNA (viral load). Women should continue their antepartum ARV regimen on schedule as much as possible during the intrapartum period to maintain maximal virologic suppression and to minimize the chance of developing drug resistance. When cesarean delivery is planned, oral medications can be administered preoperatively with sips of water. Medications that must be taken with food for absorption can be taken with liquid dietary supplements, contingent on consultation with the attending anesthesiologist during the preoperative period. If the maternal ARV drug regimen must be interrupted temporarily (meaning for <24 hours) during the peripartum period, all drugs should be stopped and reinstated simultaneously to minimize the chance that resistance will develop.

### **Decisions Regarding the Use of Intrapartum Intravenous Zidovudine**

Intrapartum administration of IV ZDV provides antiretroviral pre-exposure prophylaxis at a time when infants are at increased risk of exposure to maternal blood and body fluids. Although the PACTG 076 ZDV regimen included a continuous IV infusion of ZDV during labor for all women, decisions regarding the use of IV ZDV during labor are now based on maternal ART, HIV RNA level, and adherence considerations (see [Table 7](#) below). IV ZDV is also recommended for women with an initial diagnosis of HIV during labor and women with HIV whose HIV RNA level is unknown.

Current evidence indicates that intrapartum IV ZDV reduces perinatal HIV transmission for women with HIV RNA >1,000 copies/mL who are on ART, but the benefits for women with HIV RNA ≤1,000 copies/mL are less clear. Using data from 1997 to 2010, the French Perinatal Cohort Study evaluated the association between

IV ZDV and perinatal HIV transmission based on HIV RNA levels in >11,000 pregnant women with HIV who were on ART (72% of the women received triple-ARV regimens). The majority of the women (95%) received IV intrapartum ZDV.<sup>6</sup> Among women with HIV RNA  $\geq$ 1,000 copies/mL whose infants received only ZDV for prophylaxis, the risk of perinatal HIV transmission was significantly higher without maternal IV ZDV (10.2%) than with maternal IV ZDV (2.5%;  $P < 0.01$ ), but this difference was not observed if the neonate received a combination prophylaxis of two or more ARV drugs (4.8% with IV ZDV vs. 4.1% without IV ZDV,  $P = 0.83$ ). Among women with HIV RNA <1,000 copies/mL at delivery, transmission rates did not differ significantly between those who received IV ZDV (0.6%, 47 of 8,132 infants) and those who did not (0 of 369 infants,  $P > 0.20$ ).

In a European cohort of infants who were considered to be at high risk of perinatal HIV transmission, lack of IV ZDV during labor was associated with transmission on univariate analysis but not after the results were adjusted for maternal HIV RNA and other factors (adjusted odds ratio with IV ZDV was 0.79; 95% confidence interval, 0.55–1.15;  $P = 0.23$ ).<sup>7</sup> In a cohort of 717 women who delivered between 1996 and 2008 in Miami, not receiving IV ZDV during labor ( $n = 67$ ) was not associated with an increased risk of perinatal HIV transmission.<sup>8</sup> The majority of these women were receiving ART (89%) and had HIV RNA <1,000 copies/mL (75%) at delivery.

Based on available data, the Panel recommends that IV ZDV should continue to be administered to women with HIV RNA >1,000 copies/mL near delivery (or to women with HIV who have unknown HIV RNA levels), regardless of a woman's antepartum ARV regimen. Though not required, administration of intrapartum IV ZDV may be considered for women with HIV RNA levels  $\geq$ 50 copies/mL and  $\leq$ 1,000 copies/mL or in women for whom there are concerns about adherence to or tolerance of their ARV regimens in late pregnancy. Many experts think the data are insufficient to determine whether administration of intrapartum IV ZDV to women with HIV RNA between 50 copies/mL and 1,000 copies/mL provides any additional protection against perinatal transmission. However, the transmission risk is slightly higher (approximately 1% to 2%) when HIV RNA is in the range of 50 copies/mL to 999 copies/mL than when it is <50 copies/mL (transmission risk is  $\leq$ 1%).<sup>1,6,9</sup>

IV ZDV is **not** required for women who meet ALL of the following three criteria: (1) are receiving ART, (2) have HIV RNA <50 copies/mL at  $\geq$ 34 to 36 weeks gestation (or 4–6 weeks before delivery), and (3) are adherent to their ARV regimen. However, a study showing that 6 percent of women with suppressed HIV RNA levels during pregnancy had viral load rebound near delivery<sup>10</sup> highlights the importance of using clinical judgement when making the decision to use intrapartum IV ZDV, regardless of the patient's viral load. The additional benefit of IV ZDV in women who are receiving ART and are virally suppressed (HIV RNA <50 copies/mL) has not been evaluated in randomized clinical trials.

If a patient has known or suspected ZDV resistance, intrapartum use of IV ZDV is still recommended in women with HIV RNA >1,000 copies/mL near delivery unless a woman has a documented history of hypersensitivity. This intrapartum use of the drug is recommended because of its proven record in reducing the risk of perinatal HIV transmission, even in the presence of maternal resistance to the drug (see [Antiretroviral Drug Resistance and Resistance Testing in Pregnancy](#)).

### **Administration of Intrapartum IV ZDV**

Intrapartum IV ZDV is recommended for women with HIV RNA >1,000 copies/mL or unknown HIV RNA near the time of delivery or when they present in labor. In women with HIV RNA >1,000 copies/mL who are undergoing a scheduled cesarean delivery for prevention of perinatal HIV transmission, IV ZDV administration should begin at least 3 hours before the scheduled cesarean delivery; **women should receive a 1-hour loading dose of ZDV at 2 mg/kg followed by a continuous IV ZDV infusion of 1 mg/kg for 2 hours (minimum of 3 hours total)**. This recommendation is based on a pharmacokinetic (PK) study in which ZDV was administered orally during pregnancy and as a continuous infusion during labor. Maternal ZDV levels were measured at

baseline, after the initial IV loading dose, and then every 3 to 4 hours until delivery. ZDV levels were also measured in cord blood.<sup>11</sup> Systemic and intracellular ZDV levels increased from baseline but appeared to stabilize after 3 hours of infusion; cord blood ZDV levels were associated with maternal levels and maternal infusion duration. If cesarean delivery is being performed for other indications and maternal viral load is  $\leq 1,000$  copies/mL near the time of delivery, administering IV ZDV is not required.

Because unscheduled cesarean delivery is performed for both maternal and fetal indications, when an unscheduled cesarean delivery is indicated in a woman who has a viral load  $>1,000$  copies/mL, consideration can be given to shortening the interval between initiation of IV ZDV administration and delivery. For example, some experts recommend administering the 1-hour loading dose of IV ZDV and not waiting to complete additional administration before proceeding with delivery when an expedited delivery is indicated.

### ***Use of Oral Intrapartum ZDV***

In some international studies, oral (rather than IV) ZDV has been administered during labor. Data are limited on the PKs of oral versus IV ZDV during labor. In studies of oral dosing in labor, ZDV levels were lower than they were with IV dosing, and PK parameters suggested erratic absorption during labor.<sup>12,13</sup> Therefore, IV administration is recommended over oral administration in the United States for women with HIV RNA  $>1,000$  copies/mL near delivery. In situations where IV administration is not possible, clinicians can consider administering oral ZDV using a 600-mg loading dose and then ZDV 400 mg every 3 hours,<sup>13</sup> although no benefit of using this approach has been proven.

## **Transmission and Mode of Delivery**

### ***Current Recommendations on Mode of Delivery***

Scheduled cesarean delivery, defined as cesarean delivery performed before the onset of labor and before rupture of membranes, is recommended at 38 weeks gestation for prevention of perinatal HIV transmission in women with HIV RNA levels  $>1,000$  copies/mL near delivery and for women with unknown HIV RNA levels. Although most studies do not specify the exact time that the HIV RNA levels closest to delivery were measured, the Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission recommends viral load testing at approximately 34 to 36 weeks gestation (4–6 weeks before delivery) to inform decisions about mode of delivery and optimal treatment of the newborn. The American College of Obstetricians and Gynecologists (ACOG) recommends that women with HIV RNA  $>1,000$  copies/mL be counseled regarding the potential benefits of scheduled cesarean delivery.<sup>14</sup>

Recommendations for cesarean delivery to prevent perinatal HIV transmission were initially based on findings from a multicenter, randomized clinical trial<sup>15</sup> and from a large individual patient data meta-analysis<sup>16</sup> that were conducted before the availability of viral load information, when most women with HIV received either no ARV drugs or ZDV as a single drug. The HIV RNA threshold of 1,000 copies/mL for decisions about mode of delivery was based largely on data from a 1999 report of the Women and Infants Transmission Study, a large prospective cohort study that reported no cases of perinatal HIV transmission among 57 women with HIV RNA levels  $<1,000$  copies/mL.<sup>17</sup> Results of studies conducted since then have been extrapolated to make current recommendations about the mode of delivery in an era when ART recommended for all pregnant women and viral load information is readily available.

In a report on births to women with HIV in the United Kingdom and Ireland between 2000 and 2011, perinatal transmission rates in women on ART with HIV RNA  $<1,000$  copies/mL who had a planned cesarean delivery (13 of 3,544; 0.3%) were not significantly different from those in women who had a planned vaginal delivery (6 of 2,238; 0.3%).<sup>9</sup> Similarly, data from the French Perinatal Cohort showed no difference in transmission rates between vaginal delivery and planned cesarean delivery among women with suppressed viral loads on ART (0.3% in both groups of women).<sup>18</sup> Among 290 deliveries in women with HIV in Finland from 1993 to

2013, 75.4 percent of women delivered vaginally, 12.5 percent delivered by elective cesarean, and 12.5 percent delivered by emergency cesarean; 80 percent had HIV RNA <50 copies/mL. No perinatal HIV transmissions occurred across the delivery methods.<sup>19</sup> For preterm deliveries in women with HIV RNA <1,000 copies/mL, **an analysis of data from the French Perinatal Cohort found that** transmission rates were slightly higher among planned vaginal deliveries than among planned cesarean deliveries, but the number of women with viral loads <400 copies/mL was low, and the differences across viral load levels were not statistically significant.<sup>18</sup>

**Given the low perinatal HIV transmission rates achievable with the use of maternal ART, the benefit of scheduled cesarean delivery is difficult to evaluate for women who are virally suppressed. It is unclear whether scheduled cesarean delivery confers any additional benefit in reducing transmission.** No evidence to date suggests any benefit from scheduled cesarean delivery in women who have been receiving ART for several weeks and who are virally suppressed at or near delivery. Furthermore, evidence exists that complication rates for cesarean deliveries are higher in women with HIV than in women without HIV.<sup>20</sup> Therefore, decisions about mode of delivery for women receiving ART with HIV RNA levels  $\leq 1,000$  copies/mL should be individualized based on discussion between an obstetrician and a pregnant woman. Women should be informed that no evidence indicates that a scheduled cesarean delivery performed solely for prevention of perinatal HIV transmission is of any benefit in women receiving ART with HIV RNA  $\leq 1,000$  copies/mL and, therefore, **is not routinely recommended** for these women.

### ***Timing of Delivery***

For the general obstetric population, ACOG recommends that a scheduled cesarean delivery not be performed before 39 weeks gestation because of the risk of iatrogenic prematurity.<sup>21,22</sup> However, when cesarean delivery is indicated to prevent transmission of HIV, ACOG recommends scheduling cesarean delivery at 38 weeks gestation to decrease the likelihood of onset of labor or rupture of membranes before delivery.<sup>14</sup> Gestational age should be determined by best obstetrical dating criteria, including last menstrual period and early ultrasound for dating purposes. Amniocentesis to document lung maturity should be avoided when possible in women with HIV.

Among 1,194 infants born to mothers with HIV, nine (1.6%) born vaginally and 18 (4.4%) delivered by scheduled cesarean had respiratory distress syndrome (RDS) ( $P < 0.001$ ). No statistically significant association existed between mode of delivery and infant RDS in an adjusted model that included infant gestational age and birth weight.<sup>23</sup> Although newborn complications may be increased with planned cesarean delivery at <39 weeks gestation, the benefits of planned cesarean delivery at 38 weeks are generally thought to outweigh the risks if the procedure is performed to prevent HIV transmission.

**In women with HIV RNA  $\leq 1,000$  copies/mL, cesarean delivery is not recommended to prevent perinatal HIV transmission. The Panel recommends that women should be delivered according to standard obstetric indications; **labor should not be induced at 38 weeks for prevention of perinatal HIV transmission.**** When scheduled cesarean delivery is performed in women with HIV RNA  $\leq 1,000$  copies/mL for an indication other than preventing HIV transmission, cesarean delivery should be scheduled based on ACOG guidelines for women without HIV. A comparison of 613 women (with HIV RNA levels <1,000 copies/mL) who delivered vaginally at 38 to 40 weeks gestation and 303 women who delivered vaginally at  $\geq 40$  weeks gestation demonstrated no difference (0.3 vs. 0.5%) in perinatal HIV transmission by estimated gestational age at delivery, which suggests that women without an indication for scheduled cesarean delivery for prevention of perinatal HIV transmission should be delivered according to standard obstetric indications.<sup>24</sup>

### ***Cesarean Delivery for Women Presenting Late in Pregnancy***

Women with HIV who present late in pregnancy and are not receiving ARV drugs may not have HIV RNA results available before delivery. Without current therapy, HIV RNA levels are unlikely to be  $\leq 1,000$  copies/

mL at baseline. Even when ART is initiated immediately, reduction in plasma HIV RNA to undetectable levels may take several weeks, depending on the baseline viral load and kinetics of viral decay for a particular drug regimen (see [Recommendations of Use of ARVs During Pregnancy and Women Who Have Not Achieved Viral Suppression on Antiretroviral Therapy](#)).<sup>25-29</sup> In this instance, scheduled cesarean delivery is likely to provide additional benefit in reducing the risk of perinatal transmission of HIV, unless viral suppression can be documented before 38 weeks gestation. Although some experts would recommend a cesarean delivery in a woman who has virologic suppression for a brief period (e.g., <2 weeks), given this scenario, many others would support a vaginal delivery as long as the woman's plasma HIV RNA level was <1,000 copies/mL by the day of delivery. No data are available to address the management of an elite controller (i.e., someone who has previously maintained an undetectable HIV RNA level without ART) who presents in labor and is not receiving ART; however, in this setting, it would appear reasonable to administer IV ZDV and allow for vaginal delivery (CIII).

### ***Risk of Maternal Complications with Cesarean Delivery***

Administration of perioperative antimicrobial prophylaxis is recommended for all women to decrease maternal infectious morbidity associated with cesarean delivery. Most studies performed in the era before routine ART was recommended demonstrated that women with HIV have higher rates of postoperative complications (mostly infectious) than women without HIV and that their risk of complications is related to degree of immunosuppression and the receipt of suppressive ART.<sup>30-35</sup> A Cochrane review of six studies in women with HIV concluded that urgent cesarean delivery was associated with the highest risk of postpartum morbidity, scheduled cesarean delivery was intermediate in risk, and vaginal delivery had the lowest risk of morbidity.<sup>36,37</sup> Complication rates in women with HIV in most studies<sup>15,38-42</sup> were within the range reported in populations of women without HIV with similar risk factors and not of sufficient frequency or severity to outweigh the potential benefit of reduced perinatal HIV transmission.

A U.S. study of nationally representative data from a large administrative database demonstrated that—even in the era of ART—infectious complications, surgical trauma, prolonged hospitalization, and in-hospital deaths remain higher among women with HIV than among women without HIV.<sup>20</sup> The rate of any complication associated with cesarean delivery was 117 per 1,000 deliveries among women with HIV and 67 per 1,000 deliveries among women without HIV. A meta-analysis of primarily observational studies in women with HIV also reported higher morbidity with elective cesarean delivery than with vaginal delivery (odds ratio [OR] 3.12) and no reduction in perinatal HIV transmission among the mothers on ART.<sup>43</sup> Therefore, women with HIV should be counseled regarding the specific risks associated with undergoing cesarean delivery in the setting of HIV infection.

In addition, caution should be exercised in proceeding with a cesarean delivery in circumstances without clear evidence of benefit, especially in younger women who are likely to have additional pregnancies and perhaps multiple cesarean deliveries. The risks of abnormal placentation (e.g., placenta previa, placenta accreta, placenta increta, placenta percreta), [bowel and bladder injury](#), and intrapartum hemorrhage increase as the number of cesarean deliveries a woman has had increases. These risks should be considered and discussed with the woman before proceeding with a cesarean delivery.<sup>44,45</sup>

### ***Managing Women Who Present in Early Labor or with Ruptured Membranes***

Most studies have shown a similar risk of perinatal HIV transmission for cesarean delivery performed for obstetric indications after labor and membrane rupture as for vaginal delivery. In one study, the HIV transmission rate was similar in women undergoing emergency cesarean delivery and those delivering vaginally (1.6% vs. 1.9%, respectively).<sup>2</sup> Although a 2001 meta-analysis found that a longer duration of ruptured membranes was associated with an increased risk of perinatal HIV transmission,<sup>46</sup> it is not clear how soon after the onset of labor or the rupture of membranes the benefit of cesarean delivery is lost for women with HIV RNA >1,000 copies/mL.<sup>47</sup> Later data on the association between the duration of rupture of membranes (ROM) and

perinatal HIV transmission in the era of ART and viral load measurement are reassuring. A prospective cohort study of 707 pregnant women in Ireland showed that among 493 women on ART with HIV RNA levels <1,000 copies/mL, no cases of perinatal transmission occurred among those with membranes ruptured for up to 25 hours. Only a viral load of >10,000 copies/mL was an independent risk factor for perinatal transmission.<sup>8</sup>

In a large, prospective, population-based surveillance study in the United Kingdom and Ireland that evaluated data on 2,116 pregnancies between 2007 to 2012, there was no difference in perinatal HIV transmission between women with a ROM duration of  $\geq 4$  hours (0.64%) and those with a ROM duration of <4 hours (0.34%). Among women with HIV RNA <50 copies/mL, the transmission rate for a ROM duration  $\geq 4$  hours was 0.14% and did not differ from the rate for a ROM duration of <4 hours (0.12%). The median duration of ROM was 3 hours 30 minutes (interquartile range [IQR] 1–8 hours). The infants in this study were delivered at term, vaginally or by emergency cesarean delivery, to women with HIV who were on ART; the majority of women (89%) had HIV RNA <50 copies/mL and only 1 percent of them had HIV RNA  $\geq 1,000$  copies/mL. Among preterm infants, no transmissions occurred during 163 deliveries where the maternal viral load was <50 copies/mL.<sup>48</sup>

Because it is not clear whether cesarean delivery after onset of labor reduces the risk of perinatal HIV transmission in women with HIV RNA >1,000 copies/mL, management of women originally scheduled for cesarean delivery who present in labor or with ruptured membranes must be individualized at the time of presentation. In these circumstances, consultation with an expert in perinatal HIV may be helpful. Because the delivery plan in the setting of labor must be made quickly, telephone consultation via a 24 hour, 7-day-a-week hotline (e.g., the National Perinatal HIV/AIDS Clinical Consultation Center [1 888-448-8765]) may provide assistance in rapidly developing an individualized plan.

If spontaneous ROM occurs at >34 weeks gestation before labor or early in labor in women whose HIV RNA level is  $\leq 1,000$  copies/mL, interventions to decrease the interval to delivery (e.g., administration of oxytocin) should be considered based on obstetric considerations. When membrane rupture occurs before 34 weeks gestation, decisions about timing of delivery should be based on best obstetric practices, considering risks to the infant of prematurity and of HIV transmission. Steroids should be given, when appropriate, to accelerate fetal lung maturity because no data exist to suggest that these recommendations need to be altered for women with HIV.

## Other Intrapartum Management

### **Obstetric Procedures**

Obstetric procedures that increase the risk of fetal exposure to maternal blood, such as invasive fetal monitoring, have been associated with an increased risk of perinatal transmission in some studies, primarily those performed in the pre-ART era.<sup>49-52</sup> Data are limited on the use of fetal scalp electrodes during labor in women who are receiving suppressive ART and who have an undetectable viral load. The use of fetal scalp electrodes for fetal monitoring is an additional source of perinatal HIV exposure for the infant and should be avoided in the setting of maternal HIV infection when possible. If a fetal scalp electrode is used, some Panel members would manage the infant as being at high risk of perinatal HIV transmission even when the mother is virally suppressed (HIV RNA <50 copies/mL). See [Antiretroviral Management of Newborns with Perinatal HIV Exposure or Perinatal HIV](#).

Based on data discussed in the previous section (see Managing Women Who Present in Early Labor or with Ruptured Membranes), artificial ROM can be performed for standard obstetric indications in women with HIV RNA <50 copies/mL who are on ART and are virally suppressed. Artificial ROM should be avoided in women with HIV RNA  $\geq 50$  copies/mL, unless there is a clear obstetric indication. Although no data exist about the risks of perinatal HIV transmission with intrauterine pressure catheters, clinicians may use them with caution when indicated.

Delayed cord clamping has been associated with improved iron stores in both term and preterm infants, as well as a lower incidence of necrotizing enterocolitis and intraventricular hemorrhage in preterm infants born to mothers without HIV. ACOG now recommends delaying cord clamping for 30 to 60 seconds after birth in vigorous term and preterm infants.<sup>53-55</sup> In the setting of HIV infection, a recent study of 64 mother-infant pairs in which 32 infants had early cord clamping (performed <30 seconds after birth) and 32 infants had delayed cord clamping (performed 120 seconds after birth) found that mean hemoglobin levels at 24 hours of life were significantly higher in the delayed cord clamping group ( $P = 0.05$ ). This difference persisted at 1 month of age ( $P < 0.05$ ), despite differential prescribing of iron supplementation to infants with anemia. All mothers were on stable ARV regimens. During 18 months of follow up, there were no HIV transmissions and no increased risk of jaundice or polycythemia in infants with delayed cord clamping.<sup>56</sup>

### ***Intrapartum Epidural Use and Pharmacologic Interactions with ARV Drugs***

Ritonavir (RTV) inhibition of cytochrome P450 (CYP) 3A4 decreases the elimination of fentanyl by 67 percent. This raises concerns about a possible increased risk of respiratory depression, particularly with patient-controlled analgesia during labor, in women who are receiving regimens that contain RTV. However, a pharmacokinetic simulation study suggested that even with maximal clinical dosing regimens of epidural fentanyl over 24 hours, RTV-induced CYP3A4 inhibition is unlikely to produce the plasma fentanyl concentrations that are associated with a decrease in minute ventilation.<sup>57</sup> This suggests that epidural anesthesia can be used safely regardless of a patient's ARV regimen.

### ***Operative Vaginal Delivery***

In the past, before data from the era of ART was available, HIV was considered a relative contraindication to operative vaginal delivery with forceps or vacuum device. Peters et al. reviewed the deliveries of 9,072 women with HIV in the United Kingdom between 2008 and 2016. The percentage of women with viral suppression was 80 percent for the deliveries from 2007 through 2011 and 90 percent for those from 2012 through 2014. Among the 3,023 of 3,663 vaginal deliveries with data as to whether forceps or vacuum device were used, 249 (8.2%) involved operative delivery (5.6% using forceps, 2.4% using vacuum device, 0.1% using both forceps and vacuum device, and 0.2% device type unknown). Among the 222 infants with known HIV status at 18 months of age, there was one case of HIV transmission with multiple possible causes and not enough evidence to confirm intrapartum transmission. The study authors concluded that operative delivery is a safe option for women who are virally suppressed.<sup>58</sup> Based on these data, the Panel recommends that operative delivery with forceps or a vacuum extractor should follow standard obstetric indications but should be avoided, if possible, when HIV RNA is  $\geq 50$  copies/mL. No data from the ART era address the risk of perinatal HIV transmission associated with episiotomy or with vaginal or perineal tears in the absence of maternal viremia; indications for episiotomy should be the same as they are for women without HIV (e.g., a need for expedited vaginal delivery, a need for operative vaginal delivery, shoulder dystocia).

### ***Postpartum Hemorrhage, ARV Drugs, and Methergine Use***

Oral or parenteral methergine or other ergot alkaloids are often used as first-line treatment for postpartum hemorrhage caused by uterine atony. However, methergine should not be coadministered with drugs that are potent CYP3A4 enzyme inhibitors, including protease inhibitors (PIs). Concomitant use of ergotamines with PIs and/or cobicistat (COBI) has been associated with exaggerated vasoconstrictive responses.<sup>59</sup> When uterine atony results in excessive postpartum bleeding in women who are receiving PIs or COBI, methergine should be used only if alternative treatments, such as prostaglandin F<sub>2</sub>-alpha, misoprostol, or oxytocin, are unavailable or are contraindicated. If no alternative medications are available and the need for pharmacologic treatment outweighs the risks, methergine should be used at the lowest effective dose for the shortest possible duration. In contrast, additional uterotonic agents may be needed when using other ARV drugs that are CYP3A4 inducers (e.g., nevirapine, efavirenz, etravirine) because of the potential for decreased methergine levels and inadequate treatment effect. No known drug-drug interactions limit the adjunctive use of tranexamic acid in this setting.

**Table 7. Intrapartum Care and Recommended Interventions to Prevent Perinatal HIV Transmission for Women with HIV, Based on Maternal HIV RNA Levels at the Time of Delivery**

All women with HIV should be receiving antiretroviral therapy (ART) or initiate ART in pregnancy as early as possible to suppress HIV RNA to undetectable levels (<50 copies/mL).

Maternal HIV RNA at Time of Delivery Assessed at $\geq 34$ to 36 Weeks Gestation (or 4–6 Weeks Before Delivery) with No Concerns Regarding ART Adherence <sup>a</sup>				
	<50 copies/mL and on ART with No Concerns About Adherence	$\geq 50$ to $\leq 1,000$ copies/mL	>1,000 copies/mL	<ul style="list-style-type: none"> <li>Unknown HIV RNA</li> <li>ART Adherence Concerns</li> <li>Not Receiving ART</li> <li>HIV Diagnosis in Labor</li> </ul>
<b>Intrapartum ART</b>	Women 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 women diagnosed with HIV during labor.			
<b>Intrapartum IV ZDV</b>	Not required (BII).	Not required but may be considered (CII); many experts recommend.	Yes, recommended (AI). <sup>b</sup>  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).	
<b>Mode of delivery</b>	Normal vaginal delivery <sup>c</sup> (AII).	Normal vaginal delivery <sup>c</sup> (AII).	Scheduled cesarean delivery at 38 weeks <sup>d</sup> (AII).	Individualized care, see footnote. <sup>d</sup>
<b>Artificial rupture of membranes<sup>e</sup></b>	Per standard obstetric indications (BII).	Avoid if possible (BIII).	Not applicable, cesarean delivery recommended.	Avoid if possible in women with detectable or unknown viral load who are not receiving a cesarean delivery (BIII).
<b>Induction of labor</b>	Per standard obstetric indications, including use of pitocin. <b>Women with HIV RNA <math>\leq 1,000</math> copies/mL should NOT be routinely induced at 38 weeks.</b>		Not applicable, scheduled cesarean delivery recommended.	Avoid if possible (BIII).
<b>IUPC</b>	Data not available for women with HIV; use IUPC with caution and only if there are clear obstetric indications.			

Maternal HIV RNA at Time of Delivery				
Assessed at $\geq 34$ to 36 Weeks Gestation (or 4–6 Weeks Before Delivery) with No Concerns Regarding ART Adherence <sup>a</sup>				
	<50 copies/mL and on ART with No Concerns About Adherence	$\geq 50$ to $\leq 1,000$ copies/mL	>1,000 copies/mL	<ul style="list-style-type: none"> <li>Unknown HIV RNA</li> <li>ART Adherence Concerns</li> <li>Not Receiving ART</li> <li>HIV Diagnosis in Labor</li> </ul>
<b>Fetal scalp electrodes for fetal monitoring</b>	Avoid, particularly when maternal viral load is not suppressed ( $\geq 50$ copies/mL) or is unknown, because of the potential risk of HIV transmission (BIII). See <a href="#">Antiretroviral Management of Newborns with Perinatal HIV Exposure or Perinatal HIV</a> .			
<b>Operative delivery with forceps or a vacuum extractor</b>	Per standard obstetric indications (BIII).	Avoid for women in the setting of viremia if possible (BIII).		
<b>Delayed cord clamping</b>	Per standard obstetric indications and care.			
<b>Use of methergine for postpartum hemorrhage</b>	Because of potential drug interactions with some ARV drugs, consider a woman's ARV regimen when treating postpartum bleeding caused by uterine atony (BIII). <sup>f</sup>			
<b>Infant ARVs and infant feeding</b>	See <a href="#">Antiretroviral Management of Newborns with Perinatal HIV Exposure or Perinatal HIV</a> , <a href="#">Table 8</a> , <a href="#">Table 9</a> , <a href="#">Postpartum Care</a> , and <a href="#">Guidelines for Counseling and Managing Women with HIV in the United States Who Desire to Breastfeed</a> .			

**Key:** ART = antiretroviral therapy; CYP3A4 = cytochrome P450 3A4; HIV = human immunodeficiency virus; IUPC = intrauterine pressure catheter; IV = intravenous; RNA = ribonucleic acid; ZDV = zidovudine

<sup>a</sup> Assess ART adherence at every visit and upon presentation for delivery.

<sup>b</sup> Begin IV ZDV when women present in labor or at least 3 hours before a cesarean delivery using a 1-hour loading dose of ZDV at 2 mg/kg followed by a continuous ZDV infusion of 1 mg/kg for at least 2 hours (AII).

<sup>c</sup> Scheduled cesarean delivery performed solely for prevention of perinatal HIV transmission in women receiving ART with HIV RNA  $\leq 1,000$  copies/mL **is not recommended** given the low rate of perinatal transmission in this group (AII). In women with HIV RNA levels  $\leq 1,000$  copies/mL, if scheduled cesarean delivery or induction is indicated, it should be performed at the standard time for obstetric indications (AII).

<sup>d</sup> Provide individualized care. If HIV RNA is  $>1,000$  copies/mL or unknown, evidence is insufficient to determine whether cesarean delivery reduces the risk of perinatal HIV transmission for women who present in spontaneous labor or with ruptured membranes. Management of women originally scheduled for cesarean delivery because of HIV who present in labor must be individualized at the time of presentation (BII). In these circumstances, consultation with an expert in perinatal HIV (e.g., telephone consultation with the National Perinatal HIV/AIDS Clinical Consultation Center at 1-888-448-8765) may be helpful in rapidly developing an individualized plan.

<sup>e</sup> In women on ART with suppressed viral load (HIV RNA  $<50$  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 (BII).

<sup>f</sup> Consider drug interactions with ART when treating postpartum bleeding caused by uterine atony. In women who are receiving a cytochrome P450 3A4 enzyme inhibitor (e.g., a protease inhibitor, cobicistat), methergine should be used only if no alternative treatments for postpartum hemorrhage are available and the need for pharmacologic treatment outweighs the risks. If methergine is used, it should be administered at the lowest effective dose for the shortest possible duration (**BIII**). In women who are receiving a CYP3A4 enzyme inducer if, such as nevirapine, efavirenz, or etravirine, additional uterotonic agents may be needed because of the potential for decreased methergine levels and inadequate treatment effect (**BIII**).

**Rating of Recommendations:** A = Strong; B = Moderate; C = Optional

**Rating of Evidence:** I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

## References

1. Myer L, Phillips TK, McIntyre JA, et al. HIV viraemia and mother-to-child transmission risk after antiretroviral therapy initiation in pregnancy in Cape Town, South Africa. *HIV Med.* 2017;18(2):80-88. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27353189>.
2. Townsend CL, Cortina-Borja M, Peckham CS, de Ruiter A, Lyall H, Tookey PA. Low rates of mother-to-child transmission of HIV following effective pregnancy interventions in the United Kingdom and Ireland, 2000-2006. *AIDS.* 2008;22(8):973-981. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/18453857>.
3. Mandelbrot L, Tubiana R, Le Chenadec J, et al. No perinatal HIV-1 transmission from women with effective antiretroviral therapy starting before conception. *Clin Infect Dis.* 2015;61(11):1715-1725. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/26197844>.
4. Branson BM, Handsfield HH, Lampe MA, et al. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. *MMWR Recomm Rep.* 2006;55(RR-14):1-17; quiz CE11-14. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16988643>.
5. American College of Obstetricians Gynecologists, Committee on Obstetric Practice HIV Expert Work Group. ACOG committee opinion no. 752: prenatal and perinatal human immunodeficiency virus testing. *Obstet Gynecol.* 2018;132(3):e138-e142. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/30134428>.
6. Briand N, Warszawski J, Mandelbrot L, et al. Is intrapartum intravenous zidovudine for prevention of mother-to-child HIV-1 transmission still useful in the combination antiretroviral therapy era? *Clin Infect Dis.* 2013;57(6):903-914. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23728147>.
7. Chiappini E, Galli L, Giaquinto C, et al. Use of combination neonatal prophylaxis for the prevention of mother-to-child transmission of HIV infection in European high-risk infants. *AIDS.* 2013;27(6):991-1000. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23211776>.
8. Cotter AM, Brookfield KF, Duthely LM, Gonzalez Quintero VH, Potter JE, O'Sullivan MJ. Duration of membrane rupture and risk of perinatal transmission of HIV-1 in the era of combination antiretroviral therapy. *Am J Obstet Gynecol.* 2012;207(6):482 e481-485. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23103331>.
9. Townsend CL, Byrne L, Cortina-Borja M, et al. Earlier initiation of ART and further decline in mother-to-child HIV transmission rates, 2000-2011. *AIDS.* 2014;28(7):1049-1057. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/24566097>.
10. Boucoiran I, Albert AYK, Tulloch K, et al. Human immunodeficiency virus viral load rebound near delivery in previously suppressed, combination antiretroviral therapy-treated pregnant women. *Obstet Gynecol.* 2017;130(3):497-501. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28796673>.
11. Rodman JH, Flynn PM, Robbins B, et al. Systemic pharmacokinetics and cellular pharmacology of zidovudine in human immunodeficiency virus type 1-infected women and newborn infants. *J Infect Dis.* 1999;180(6):1844-1850. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10558940>.
12. Bhadrakom C, Simonds RJ, Mei JV, et al. Oral zidovudine during labor to prevent perinatal HIV transmission, Bangkok: tolerance and zidovudine concentration in cord blood. Bangkok collaborative perinatal HIV transmission study group. *AIDS.* 2000;14(5):509-516. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10780713>.
13. Mirochnick M, Rodman JH, Robbins BL, et al. Pharmacokinetics of oral zidovudine administered during labour: a preliminary study. *HIV Med.* 2007;8(7):451-456. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/17760737>.

14. American College of Obstetricians and Gynecologists. ACOG committee opinion no. 751: labor and delivery management of women with human immunodeficiency virus infection. *Obstet Gynecol.* 2018;132(3):e131-e137. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/30134427>.
15. European Mode of Delivery Collaboration. Elective caesarean-section versus vaginal delivery in prevention of vertical HIV-1 transmission: a randomised clinical trial. *Lancet.* 1999;353(9158):1035-1039. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10199349>.
16. International Perinatal HIV Group. The mode of delivery and the risk of vertical transmission of human immunodeficiency virus type 1--a meta-analysis of 15 prospective cohort studies. The International Perinatal HIV Group. *N Engl J Med.* 1999;340(13):977-987. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10099139>.
17. Garcia PM, Kalish LA, Pitt J, et al. Maternal levels of plasma human immunodeficiency virus type 1 RNA and the risk of perinatal transmission. Women and infants transmission study group. *N Engl J Med.* 1999;341(6):394-402. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10432324>.
18. Briand N, Jasseron C, Sibiude J, et al. Cesarean section for HIV-infected women in the combination antiretroviral therapies era, 2000-2010. *Am J Obstet Gynecol.* 2013;209(4):335 e331-335 e312. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23791563>.
19. Aho I, Kaijomaa M, Kivela P, et al. Most women living with HIV can deliver vaginally: national data from Finland 1993-2013. *PLoS One.* 2018;13(3):e0194370. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29566017>.
20. Kourtis AP, Ellington S, Pazol K, Flowers L, Haddad L, Jamieson DJ. Complications of cesarean deliveries among HIV-infected women in the United States. *AIDS.* 2014;28(17):2609-2618. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/25574961>.
21. American College of Obstetricians Gynecologists. ACOG practice bulletin No. 97: fetal lung maturity. *Obstet Gynecol.* 2008;112(3):717-726. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/18757686>.
22. Tita AT, Landon MB, Spong CY, et al. Timing of elective repeat cesarean delivery at term and neonatal outcomes. *N Engl J Med.* 2009;360(2):111-120. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/19129525>.
23. Livingston EG, Huo Y, Patel K, et al. Mode of delivery and infant respiratory morbidity among infants born to HIV-1-infected women. *Obstet Gynecol.* 2010;116(2 Pt 1):335-343. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/20664394>.
24. Scott RK, Chakhtoura N, Burke MM, Cohen RA, Kreitchmann R. Delivery after 40 weeks of gestation in pregnant women with well-controlled human immunodeficiency virus. *Obstet Gynecol.* 2017;130(3):502-510. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28796679>.
25. European Collaborative Study, Patel D, Cortina-Borja M, Thorne C, Newell ML. Time to undetectable viral load after highly active antiretroviral therapy initiation among HIV-infected pregnant women. *Clin Infect Dis.* 2007;44(12):1647-1656. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/17516411>.
26. Read PJ, Mandalia S, Khan P, et al. When should HAART be initiated in pregnancy to achieve an undetectable HIV viral load by delivery? *AIDS.* 2012;26(9):1095-1103. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/22441248>.
27. Aziz N, Sokoloff A, Kornak J, et al. Time to viral load suppression in antiretroviral-naive and -experienced HIV-infected pregnant women on highly active antiretroviral therapy: implications for pregnant women presenting late in gestation. *BJOG.* 2013;120(12):1534-1547. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23924192>.

28. Alagaratnam J, Peters H, Francis K, et al. An observational study of initial HIV RNA decay following initiation of combination antiretroviral treatment during pregnancy. *AIDS Res Ther.* 2020;17(1):41. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/32660502>.
29. Kintu K, Malaba TR, Nakibuka J, et al. Dolutegravir versus efavirenz in women starting HIV therapy in late pregnancy (DolPHIN-2): an open-label, randomised controlled trial. *Lancet HIV.* 2020;7(5):e332-e339. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/32386721>.
30. Semprini AE, Castagna C, Ravizza M, et al. The incidence of complications after caesarean section in 156 HIV-positive women. *AIDS.* 1995;9(8):913-917. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/7576327>.
31. Grubert TA, Reindell D, Kastner R, Lutz-Friedrich R, Belohradsky BH, Dathe O. Complications after caesarean section in HIV-1-infected women not taking antiretroviral treatment. *Lancet.* 1999;354(9190):1612-1613. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10560681>.
32. Maiques-Montesinos V, Cervera-Sanchez J, Bellver-Pradas J, Abad-Carrascosa A, Serra-Serra V. Post-caesarean section morbidity in HIV-positive women. *Acta Obstet Gynecol Scand.* 1999;78(9):789-792. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10535342>.
33. Vimercati A, Greco P, Loverro G, Lopalco PL, Pansini V, Selvaggi L. Maternal complications after caesarean section in HIV infected women. *Eur J Obstet Gynecol Reprod Biol.* 2000;90(1):73-76. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10767514>.
34. Rodriguez EJ, Spann C, Jamieson D, Lindsay M. Postoperative morbidity associated with cesarean delivery among human immunodeficiency virus-seropositive women. *Am J Obstet Gynecol.* 2001;184(6):1108-1111. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/11349171>.
35. Urbani G, de Vries MM, Cronje HS, Niemand I, Bam RH, Beyer E. Complications associated with cesarean section in HIV-infected patients. *Int J Gynaecol Obstet.* 2001;74(1):9-15. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/11430935>.
36. Read JS, Newell MK. Efficacy and safety of cesarean delivery for prevention of mother-to-child transmission of HIV-1. *Cochrane Database Syst Rev.* 2005(4):CD005479. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16235405>.
37. Livingston EG, Huo Y, Patel K, et al. Complications and route of delivery in a large cohort study of HIV-1-infected women-IMPAACT P1025. *J Acquir Immune Defic Syndr.* 2016;73(1):74-82. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27082506>.
38. Watts DH, Lambert JS, Stiehm ER, et al. Complications according to mode of delivery among human immunodeficiency virus-infected women with CD4 lymphocyte counts of < or = 500/microL. *Am J Obstet Gynecol.* 2000;183(1):100-107. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10920316>.
39. Faucher P, Batallan A, Bastian H, et al. Management of pregnant women infected with HIV at Bichat Hospital between 1990 and 1998: analysis of 202 pregnancies. *Gynecol Obstet Fertil.* 2001;29(3):211-225. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/11300046>.
40. Fiore S, Newell ML, Thorne C, European HIV in Obstetrics Group. Higher rates of post-partum complications in HIV-infected than in uninfected women irrespective of mode of delivery. *AIDS.* 2004;18(6):933-938. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/15060441>.
41. Marcollet A, Goffinet F, Firtion G, et al. Differences in postpartum morbidity in women who are infected with the human immunodeficiency virus after elective cesarean delivery, emergency cesarean delivery, or vaginal delivery. *Am J Obstet Gynecol.* 2002;186(4):784-789. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/11967508>.

42. Read JS, Tuomala R, Kpamegan E, et al. Mode of delivery and postpartum morbidity among HIV-infected women: the women and infants transmission study. *J Acquir Immune Defic Syndr*. 2001;26(3):236-245. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/11242196>.
43. Kennedy CE, Yeh PT, Pandey S, Betran AP, Narasimhan M. Elective cesarean section for women living with HIV: a systematic review of risks and benefits. *AIDS*. 2017;31(11):1579-1591. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28481770>.
44. Silver RM, Landon MB, Rouse DJ, et al. Maternal morbidity associated with multiple repeat cesarean deliveries. *Obstet Gynecol*. 2006;107(6):1226-1232. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/16738145>.
45. Greenbaum S, Wainstock T, Dukler D, Leron E, Erez O. Underlying mechanisms of retained placenta: Evidence from a population based cohort study. *Eur J Obstet Gynecol Reprod Biol*. 2017;216:12-17. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28692888>.
46. International Perinatal HIV Group. Duration of ruptured membranes and vertical transmission of HIV-1: a meta-analysis from 15 prospective cohort studies. *AIDS*. 2001;15(3):357-368. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/11273216>.
47. Jamieson DJ, Read JS, Kourtis AP, Durant TM, Lampe MA, Dominguez KL. Cesarean delivery for HIV-infected women: recommendations and controversies. *Am J Obstet Gynecol*. 2007;197(3 Suppl):S96-100. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/17825656>.
48. Peters H, Byrne L, De Ruiter A, et al. Duration of ruptured membranes and mother-to-child HIV transmission: a prospective population-based surveillance study. *BJOG*. 2015. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/26011825>.
49. Boyer PJ, Dillon M, Navaie M, et al. Factors predictive of maternal-fetal transmission of HIV-1. Preliminary analysis of zidovudine given during pregnancy and/or delivery. *JAMA*. 1994;271(24):1925-1930. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/7911164>.
50. Mandelbrot L, Mayaux MJ, Bongain A, et al. Obstetric factors and mother-to-child transmission of human immunodeficiency virus type 1: the French perinatal cohorts. SEROGEST French Pediatric HIV Infection Study Group. *Am J Obstet Gynecol*. 1996;175(3 Pt 1):661-667. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/8828431>.
51. Mofenson LM, Lambert JS, Stiehm ER, et al. Risk factors for perinatal transmission of human immunodeficiency virus type 1 in women treated with zidovudine. Pediatric AIDS Clinical Trials Group Study 185 Team. *N Engl J Med*. 1999;341(6):385-393. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10432323>.
52. Shapiro DE, Sperling RS, Mandelbrot L, Britto P, Cunningham BE. Risk factors for perinatal human immunodeficiency virus transmission in patients receiving zidovudine prophylaxis. Pediatric AIDS Clinical Trials Group protocol 076 Study Group. *Obstet Gynecol*. 1999;94(6):897-908. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10576173>.
53. Rabe H, Diaz-Rossello JL, Duley L, Dowswell T. Effect of timing of umbilical cord clamping and other strategies to influence placental transfusion at preterm birth on maternal and infant outcomes. *Cochrane Database Syst Rev*. 2012;8:CD003248. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/22895933>.
54. McDonald SJ, Middleton P, Dowswell T, Morris PS. Effect of timing of umbilical cord clamping of term infants on maternal and neonatal outcomes. *Cochrane Database Syst Rev*. 2013;7:CD004074. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23843134>.

55. American College of Obstetricians and Gynecologists. Committee opinion No. 684: delayed umbilical cord clamping after birth. *Obstet Gynecol.* 2017;129(1):e5-e10. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28002310>.
56. Pogliani L, Erba P, Nannini P, Giacomet V, Zuccotti GV. Effects and safety of delayed versus early umbilical cord clamping in newborns of HIV-infected mothers. *J Matern Fetal Neonatal Med.* 2017:1-4. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28969479>.
57. Cambic CR, Avram MJ, Gupta DK, Wong CA. Effect of ritonavir-induced cytochrome P450 3A4 inhibition on plasma fentanyl concentrations during patient-controlled epidural labor analgesia: a pharmacokinetic simulation. *Int J Obstet Anesth.* 2014;23(1):45-51. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/24333052>.
58. Peters H, Francis K, Harding K, Tookey PA, Thorne C. Operative vaginal delivery and invasive procedures in pregnancy among women living with HIV. *Eur J Obstet Gynecol Reprod Biol.* 2017;210:295-299. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28092853>.
59. Navarro J, Curran A, Burgos J, et al. Acute leg ischaemia in an HIV-infected patient receiving antiretroviral treatment. *Antivir Ther.* 2017;22(1):89-90. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27546463>.