52 Townsend CL, Cortina-Borja M, Peckham CS, Tookey PA. Antiretroviral therapy and premature delivery in diagnosed HIV-infected women in the United Kingdom and Ireland. *AIDS* 2007; **21**: 1019–1026.

53. Beckerman K, Albano J, Cohan D *et al.* Exposure to combination antiretroviral (cARV) regimens containing protease inhibitors (PI) during pregnancy and prevalence of low birth weight/preterm delivery (LBW/PTD) among women with low pre-existing risk for LBW/PTD: a stratified analysis of 10,082 pregnancies. *6th IAS Conference on HIV Pathogenesis, Treatment and Prevention*. July 2011. Rome, Italy.

54. European Collaborative Study, Swiss Mother and Child HIV Cohort Study. Combination antiretroviral therapy and duration of pregnancy. *AIDS* 2000; **14**: 2913–2920.

55. Machado ES, Hofer CB, Costa TT *et al.* Pregnancy outcome in women infected with HIV-1 receiving combination antiretroviral therapy before versus after conception. *Sex Transm Infect* 2009; **85**: 82–87.

56. Thorne C, Patel D, Newell ML. Increased risk of adverse pregnancy outcomes in HIV-infected women treated with highly active antiretroviral therapy in Europe. *AIDS* 2004; **18**: 2337–2339.

57. Patel K, Shapiro DE, Brogly SB *et al.* Prenatal protease inhibitor use and risk of preterm birth among HIV-infected women initiating antiretroviral drugs during pregnancy. *J Infect Dis* 2010; **201**: 1035–1044.

58. Gagnon LH, MacGillivray J, Urquia ML *et al.* Antiretroviral therapy during pregnancy and risk of preterm birth. *Eur J Obstet Gynecol Reprod Biol* 2016; **201**: 51–55.

59. Lorenzi P, Spicher VM, Laubereau B *et al.* Antiretroviral therapies in pregnancy: maternal, fetal and neonatal effects. Swiss HIV Cohort Study, the Swiss Collaborative HIV and Pregnancy Study, and the Swiss Neonatal HIV Study. *AIDS* 1998; **12**: F241–247.

60. Exposure to antiretroviral therapy in utero or early life: the health of uninfected children born to HIV-infected women. *J Acquir Immune Defic Syndr* 2003; **32**: 380–387.

61. Townsend CL, Willey BA, Cortina-Borja M *et al.* Antiretroviral therapy and congenital abnormalities in infants born to HIV-infected women in the UK and Ireland, 1990-2007. *AIDS* 2009; **23**: 519–524.

62. Martin F, Taylor GP. Increased rates of preterm delivery are associated with the initiation of highly active antiretrovial therapy during pregnancy: a single-center cohort study. *J Infect Dis* 2007; **196**: 558–561.

63. Cotter AM, Garcia AG, Duthely ML *et al.* Is antiretroviral therapy during pregnancy associated with an increased risk of preterm delivery, low birth weight, or stillbirth? *J Infect Dis* 2006; **193**: 1195–1201.

64. Schulte J, Dominguez K, Sukalac T *et al.* Declines in low birth weight and preterm birth among infants who were born to HIV-infected women during an era of increased use of maternal antiretroviral drugs: Pediatric Spectrum of HIV Disease, 1989-2004. *Pediatrics* 2007; **119**: e900–906.

65. Sibiude J, Warszawski J, Tubiana R *et al.* Large increase in prematurity between 1990 and 2009 in HIV-infected women in the National ANRS French Perinatal Cohort: does ritonavir boost play a role? *Conference on Retroviruses and Opportunistic Infections*. March 2011. Boston, MA, USA.

66. Roberts SS, Martinez M, Covington DL *et al.* Lopinavir/ritonavir in pregnancy. *J Acquir Immune Defic Syndr* 2009; **51**: 456–461.

67. Samuel M, Bradshaw D, Perry M *et al.* Atazanavir in pregnancy: a report of 155 cases. *HIV Med* 2011; **12 Suppl 1**: 12.

68. Perry M, Conway K, Flanagan S *et al.* Lopinavir and atazanavir in pregnancy: comparable infant outcomes, virological efficacy and preterm delivery rates. *7th IAS Conference on HIV Pathogenesis, Treatment and Prevention*. July 2013. Kuala Lumpur, Malaysia.

69. Favarato G, Townsend CL, Bailey H *et al.* Protease inhibitors and preterm delivery: another piece in the puzzle. *AIDS* 2018; **32**: 243–252.

70. Powis KM, Kitch D, Ogwu A *et al.* Increased risk of preterm delivery among HIV-infected women randomized to protease versus nucleoside reverse transcriptase inhibitor-based HAART during pregnancy. *J Infect Dis* 2011; **204**: 506–514.

71. de Vincenzi I. Triple antiretroviral compared with zidovudine and single-dose nevirapine prophylaxis during pregnancy and breastfeeding for prevention of mother-to-child transmission of HIV-1 (Kesho Bora study): a randomised controlled trial. *Lancet Infect Dis* 2011; **11**: 171–180.

72. Cohan D, Natureeba P, Plenty A *et al.* No difference in risk of preterm birth among pregnant Ugandan women randomised to lopinavir/ritonavir vs efavirenz-based ART. *Conference on Retroviruses and Opportunistic Infections*. March 2013. Atlanta, GA, USA.

73. Siemieniuk RAC, Lytvyn L, Mah Ming J *et al.* Antiretroviral therapy in pregnant women living with HIV: a clinical practice guideline. *BMJ* 2017; **358**: j3961.

74. Feghali M, Venkataramanan R, Caritis S. Pharmacokinetics of drugs in pregnancy. *Semin Perinatol* 2015; **39**: 512–519.

75. 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**: 1844–1850.

76. Moodley J, Moodley D, Pillay K *et al.* Pharmacokinetics and antiretroviral activity of lamivudine alone or when coadministered with zidovudine in human immunodeficiency virus type 1-infected pregnant women and their offspring. *J Infect Dis* 1998; **178**: 1327–1333.

77. Best BM, Mirochnick M, Capparelli EV *et al.* Impact of pregnancy on abacavir pharmacokinetics. *AIDS* 2006; **20**: 553–560.

78. Burchett S, Best B, Mirochnick M *et al.* Tenofovir pharmacokinetics during pregnancy, at delivery and post partum. *Conference on Retroviruses and Opportunistic Infections*. February 2007. Los Angeles, CA, USA.

79. Colbers AP, Hawkins DA, Gingelmaier A *et al.* The pharmacokinetics, safety and efficacy of tenofovir and emtricitabine in HIV-1-infected pregnant women. *AIDS* 2013; **27**: 739–748.

80. Benaboud S, Hirt D, Launay O *et al.* Pregnancy-related effects on tenofovir pharmacokinetics: a population study with 186 women. *Antimicrob Agents Chemother* 2012; **56**: 857–862.

81. Mirochnick M, Taha T, Kreitchmann R *et al.* Pharmacokinetics and safety of tenofovir in HIV-infected women during labor and their infants during the first week of life. *J Acquir Immune Defic Syndr* 2014; **65**: 33–41.

82. Hodder S, Squires K, Kityo C *et al.* Efficacy and safety of switching to EVG/cobi/FTC/TAF in virologically suppressed women. *Conference on Retroviruses and Opportunistic Infections*. February 2017. Seattle, WA, USA.

83. Stek AM, Best BM, Luo W *et al.* Effect of pregnancy on emtricitabine pharmacokinetics. *HIV Med* 2012; **13**: 226–235.

84. Colbers A, Schalkwijk S, Konopnick D *et al.* Substantially lower rilpivirine plasma concentrations during pregnancy. *Conference on Retroviruses and Opportunistic Infections*. February 2017. Seattle, WA, USA.

85 Cressey T, Stek A, Capparelli E *et al.* Efavirenz pharmacokinetics during the 3rd trimester of pregnancy and postpartum. *Conference on Retroviruses and Opportunistic Infections*. March 2011. Boston, MA, USA.

86. Ramgopal M, Osiyemi O, Zorrilla C *et al.* Pharmacokinetics of total and unbound etravirine in HIV-1-infected pregnant women. *J Acquir Immune Defic Syndr* 2016; **73**: 268–274.

87. Best BM, Colbers A, Wang J *et al.* Etravirine pharmacokinetics during pregnancy and postpartum. *Conference on Retroviruses and Opportunistic Infections*. February 2015. Seattle, WA, USA.

88. Taylor GP, Lyall EG, Back D *et al.* Pharmacological implications of lengthened in-utero exposure to nevirapine. *Lancet* 2000; **355**: 2134–2135.

89. Colbers A, Molto J, Ivanovir J *et al.* A comparison of the pharmacokinetics of raltegravir during pregnancy and post-partum. *12th International Workshop on Clinical Pharmacology of HIV Therapy*. April 2011. Miami, FL, USA.

90. Belissa E, Benchikh A, Charpentier C *et al.* Raltegravir plasma concentrations on HIV-1 infected pregnant women. *Conference on Retroviruses and Opportunistic Infections*. February 2015. Seattle, WA, USA.

91. Blonk M, Colbers A, Hidalgo-Tenorio C *et al.* A comparison of the pharmacokinetics of raltegravir during pregnancy and postpartum. *Conference on Retroviruses and Opportunistic Infections*. March 2014. Boston, MA, USA.

92. Jeantils V, Messaouden H, Carbillon L. Pregnancy and a regimen containing raltegravir: a pilot study on the materno-foetal safety. *53rd International Conference on Antibiotics and Antimicrobial Chemotherap*. September 2013. Denver, Co, USA.

93. Best B, Capparelli E, Stek A *et al.* Elvitegravir/cobicistat pharmacokinetics in pregnancy and postpartum. *Conference on Retroviriuses and Opportunistic Infections*. February 2017. Seattle, WA, USA.

94. Mulligan N, Best B, Capparelli E *et al.* Dolutegravir pharmacokinetics in HIV-infected pregnant and postpartum women. *Conference on Retroviruses and Opportunistic Infections*. February 2016. Boston, MA, USA. Abstract 438.

95. Medicines and Healthcare products Regulatory Agency. *Darunavir boosted with cobicistat: avoid use in pregnancy due to risk of treatment failure and maternal-to-child transmission of HIV-1*. July 2018. Available at: www.gov.uk/drug-safety-update/darunavir-boosted-with-cobicistat-avoid-use-in-pregnancy-due-to-risk-of-treatment-failure-and-maternal-to-child-transmission-of-hiv-1 (accessed October 2018).

96. Aweeka FT, Stek A, Best BM *et al.* Lopinavir protein binding in HIV-1-infected pregnant women. *HIV Med* 2010; **11**: 232–238.

97. Best BM, Stek AM, Mirochnick M *et al.* Lopinavir tablet pharmacokinetics with an increased dose during pregnancy. *J Acquir Immune Defic Syndr* 2010; **54**: 381–388.

98. Else LJ, Douglas M, Dickinson L *et al.* Improved oral bioavailability of lopinavir in melt-extruded tablet formulation reduces impact of third trimester on lopinavir plasma concentrations. *Antimicrob Agents Chemother* 2012; **56**: 816–824.

99. Ripamonti D, Cattaneo D, Maggiolo F *et al.* Atazanavir plus low-dose ritonavir in pregnancy: pharmacokinetics and placental transfer. *AIDS* 2007; **21**: 2409–2415.

100. Mirochnick M, Best BM, Stek AM *et al.* Atazanavir pharmacokinetics with and without tenofovir during pregnancy. *J Acquir Immune Defic Syndr* 2011; **56**: 412–419.

101. Eley T, Bertz R, Hardy H, Burger D. Atazanavir pharmacokinetics, efficacy and safety in pregnancy: a systematic review. *Antivir Ther* 2013; **18**: 361–375.

102. Colbers A, Hawkins D, Hidalgo-Tenorio C *et al.* Atazanavir exposure is effective during pregnancy regardless of tenofovir use. *Antivir Ther* 2015; **20**: 57–64.

103. Conradie F, Zorrilla C, Josipovic D *et al.* Safety and exposure of once-daily ritonavir-boosted atazanavir in HIV-infected pregnant women. *HIV Med* 2011; **12**: 570–579.

104. Stek A, Best BM, Wang J *et al.* Pharmacokinetics of once versus twice daily darunavir in pregnant HIV-infected women. *J Acquir Immune Defic Syndr* 2015; **70**: 33–41.

105. Colbers A, Molto J, Ivanovic J *et al.* A comparison of the pharmacokinetics of darunavir, atazanavir and ritonavir during pregnancy and post-partum. *Conference on Retroviruses and Opportunistic Infections*. March 2012. Seattle, WA, USA.

106. Zorrilla CD, Wright R, Osiyemi OO *et al.* Total and unbound darunavir pharmacokinetics in pregnant women infected with HIV-1: results of a study of darunavir/ritonavir 600/100 mg administered twice daily. *HIV Med* 2014; **15**: 50–56.

107. Crauwels HM, Kakuda TN, Ryan B *et al.* Pharmacokinetics of once-daily darunavir/ritonavir in HIV-1-infected pregnant women. *HIV Med* 2016; **17**: 643–652.

108. Stek A, Best B, Capparelli E *et al.* Pharmacokinetics of increased dose darunavir during late pregnancy and postpartum. *Conference on Retroviruses and Opportunistic Infections*. February 2016. Boston, MA, USA.

109. Ceccaldi PF, Ferreira C, Gavard L *et al.* Placental transfer of enfuvirtide in the *ex vivo* human placenta perfusion model. *Am J Obstet Gynecol* 2008; **198**: 433.e1–2.

110. Comparison of vertical human immunodeficiency virus type 2 and human immunodeficiency virus type 1 transmission in the French prospective cohort. The HIV Infection in Newborns French Collaborative Study Group. *Pediatr Infect Dis J* 1994; **13**: 502-506.

111. Adjorlolo-Johnson G, De Cock KM, Ekpini E *et al.* Prospective comparison of mother-to-child transmission of HIV-1 and HIV-2 in Abidjan, Ivory Coast. *JAMA* 1994; **272**: 462–466.

112. O'Donovan D, Ariyoshi K, Milligan P *et al.* Maternal plasma viral RNA levels determine marked differences in mother-to-child transmission rates of HIV-1 and HIV-2 in The Gambia. MRC/Gambia Government/University College London Medical School working group on mother-child transmission of HIV. *AIDS* 2000; **14**: 441–448.

113. Roquebert B, Damond F, Collin G *et al.* HIV-2 integrase gene polymorphism and phenotypic susceptibility of HIV-2 clinical isolates to the integrase inhibitors raltegravir and elvitegravir in vitro. *J Antimicrob Chemother* 2008; **62**: 914–920.

7. HIV and hepatitis virus co-infections

7.1 Hepatitis B virus (HBV)

The combination of HIV, chronic HBV infection and pregnancy presents unique management considerations. Referral to the local designated specialist should be undertaken to ensure that all aspects of care are addressed, including the effects of HBV/HIV on pregnancy, effects of pregnancy on the course of co-infection, antiretroviral management for both HBV and HIV, and prevention of vertical transmission for both viruses. Pregnant women with advanced cirrhosis should be managed in a tertiary centre with a hepatologist.

The prevalence of HBV co-infection in pregnant women tends to reflect that of the adult population (Europe/Africa 4–10%) [1-4] and is 40% higher than that found in the general population (HIV positive *vs* HIV negative: relative risk [RR] 1.40; 95% CI 1.16–1.69) [1]. Up to one-third of hepatitis B surface antigen (HBsAg) is wild-type (hepatitis B envelope antigen [HBeAg] positive) and, depending on region, up to 6% of individuals may be co-infected with hepatitis delta virus. Rates of HBV/HIV co-infection vary with race and ethnicity so that changing immigration patterns in Western countries with traditionally low prevalence may significantly influence rates at a regional level (e.g. 6% among Asian women in the USA *vs* 0.6% in white women) [5]. The same is true for injecting drug use (prevalence <0.1% in Northwestern Europe compared to 1–4% in Southern Europe) and sexual transmission (prevalence is higher in men who have sex with men).

Although plausible because of higher levels of HBV DNA in women living with both HBV and HIV, there is no evidence of increased vertical transmission of HBV in co-infection compared with mono-infection. The impact of pregnancy on women with HBV mono-infection is small. There appears to be no worsening of liver disease in the majority of women, although case reports of hepatic exacerbations/fulminant hepatic failure have been reported; alanine transaminase (ALT) levels tend to fall, HBeAg seroconversion occurs in a small minority and may be associated with liver dysfunction, and HBV DNA levels may rise by as much as 1 $\log_{10}$ unit. The impact of HBV infection on pregnancy appears negligible.

By contrast, the effect of HIV on HBV disease progression includes higher levels of HBV replication (HBV DNA levels and proportion HBeAg positive), higher mortality when compared to HIV or HBV mono-infection, a higher rate of chronicity (20–80% compared to 3–5% in HIV-negative individuals with risk increasing with lower CD4 cell counts at the time of HBV acquisition), lower ALT levels, higher rate of hepatoma, lower rate of spontaneous loss of HBeAg or HBsAg and seroconversion to anti-HBe and anti-HBs, faster progression to cirrhosis, and a higher incidence of lamivudine resistance [6].

7.1.1	On diagnosis of new HBV infection, confirmation of viraemia with quantitative HBV DNA, ‘e’ antigen status as well as hepatitis A virus (HAV), HCV and hepatitis D virus (HDV) screening and tests to assess hepatic inflammation/fibrosis and liver function are recommended.	1C
7.1.2	LFTs should be repeated at 2 and 4 weeks after commencing ART to detect evidence of hepatotoxicity or immune reconstitution inflammatory syndrome (IRIS) and then monitored regularly throughout pregnancy and postpartum.	1C

In a pregnant woman living with HIV and newly diagnosed with HBV (HBsAg positive on antenatal screening or diagnosed preconception), baseline hepatitis B markers (anti-HBc/HBeAg/anti-HBe status) and level of the virus (HBV DNA), the degree of inflammation and synthetic function (ALT, aspartate transaminase [AST], albumin and international normalised ratio [INR]), an assessment of fibrosis and the exclusion of additional causes of liver disease (e.g. haemochromatosis and autoimmune hepatitis) are indicated. Additionally, patients should be assessed for the need for HAV immunisation, by testing for HAV immunoglobulin (Ig)G antibody, as well as for HDV co-infection (HDV serology and HDV RNA if positive).

Liver biopsy and hepatic elastometry (FibroScan) are relatively contraindicated during pregnancy [7], therefore clinical assessment, use of blood panel-based fibrosis markers (e.g. aspartate aminotransferase-to-platelet ratio