Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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Table 12d. Antiretroviral-Therapy-Associated Adverse Effects and Management Recommendations—Hematologic Effects (Last updated March 1, 2016; last reviewed March 1, 2016) (page 1 of 2)

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
Anemia[a]	Principally ZDV	Onset: • Variable, weeks to months Presentation *Most Commonly:* • Asymptomatic or mild fatigue • Pallor • Tachypnea *Rarely:* • Congestive heart failure	HIV-Exposed Newborns: • Severe anemia is uncommon, but may be seen coincident with physiologic Hgb nadir. HIV-Infected Children on ARVs: • 2–3 times more common with ZDV-containing regimens; less frequent with currently recommended dosing of ZDV	HIV-Exposed Newborns: • Premature birth • *In utero* exposure to ARVs • Advanced maternal HIV • Neonatal blood loss • Combination ARV prophylaxis, particularly with ZDV plus 3TC HIV-Infected Children on ARVs: • Underlying hemoglobinopathy (e.g., sickle cell disease, G6PD deficiency) • Myelosuppressive drugs (e.g., TMP-SMX, rifabutin) • Iron deficiency • Advanced or poorly controlled HIV disease • Malnutrition	HIV-Exposed Newborns: • Obtain CBC at birth. • Consider repeat CBC at 4 weeks for neonates who are at higher risk (e.g., those born prematurely or known to have low birth Hgb). HIV-Infected Children on ARVs: • Avoid ZDV in children with moderate to severe anemia when alternative agents are available. • Obtain CBC as part of routine care.	HIV-Exposed Newborns: • Rarely require intervention unless Hgb is <7.0 g/dL or anemia is associated with symptoms. • Consider discontinuing ZDV if 4 weeks or more of a 6-week ZDV prophylaxis regimen are already completed (see the Perinatal Guidelines[b]). HIV-Infected Children on ARVs: • Discontinue non-ARV, marrow-toxic drugs, if feasible. • Treat coexisting iron deficiency, OIs, malignancies. • For persistent severe anemia thought to be associated with ARVs, change to a non-ZDV-containing regimen; consider a trial of erythropoietin if essential to continue ZDV.
Macrocytosis	Principally ZDV; also d4T	Onset: • Within days to weeks of starting therapy • MCV often >100 fL Presentation: • Most often asymptomatic • Sometimes associated with anemia (occurs more often with ZDV than with d4T)	>90% to 95%, all ages	None	Obtain CBC as part of routine care.	None required unless associated with anemia

Table 12d. Antiretroviral-Therapy-Associated Adverse Effects and Management Recommendations—Hematologic Effects (Last updated March 1, 2016; last reviewed March 1, 2016) (page 2 of 2)

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
Neutropenia[a]	Principally ZDV	Onset: • Variable Presentation: • Most commonly asymptomatic. Complications appear to be less than with neutropenias associated with cancer chemotherapy.	HIV-Exposed Newborns: • Rare HIV-Infected Children on ARVs: • 2.2% to 26.8% of children on ARVs, depending upon the ARV regimen. 2.2% for ZDV/3TC • Highest rates with ZDV-containing regimens	HIV-Exposed Newborns: • *In utero* exposure to ARVs • Combination ARV prophylaxis, particularly with ZDV plus 3TC HIV-Infected Children on ARVs: • Advanced or poorly controlled HIV infection • Myelosuppressive drugs (e.g., TMP-SMX, ganciclovir, hydroxyurea, rifabutin)	HIV-Infected Children on ARVs: • Obtain CBC as part of routine care.	HIV-Exposed Newborns: • No established threshold for intervention; some experts would consider using an alternative NRTI for prophylaxis if ANC <500 cells/mm^3, or discontinue ARV prophylaxis entirely if ≥4 weeks of 6-week ZDV prophylaxis have been completed (see the Perinatal Guidelines[b]). HIV-Infected Children on ARVs: • Discontinue non-ARV marrow-toxic drugs, if feasible. • Treat coexisting OIs and malignancies. • For persistent severe neutropenia thought to be associated with ARVs, change to a non-ZDV-containing regimen. Consider a trial of G-CSF if essential to continue ZDV.

[a] HIV infection itself, OIs, and medications used to prevent OIs, such as TMP-SMX, may all contribute to anemia, neutropenia, and thrombocytopenia.

[b] *Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States*

Key to Acronyms: 3TC = lamivudine; ANC = absolute neutrophil count; ARV = antiretroviral; CBC = complete blood count; d4t = stavudine; dL = deciliter; fL = femtoliter; G6PD = glucose-6-phosphate dehydrogenase; G-CSF = granulocyte colony-stimulating factor; Hgb = hemoglobin; MCV = mean cell volume; NRTI = nucleoside reverse transcriptase inhibitor; OI = opportunistic infection; TMP-SMX = trimethoprim-sulfamethoxazole; ZDV = zidovudine

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