Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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Table 15d. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Hematologic Effects (Last updated April 16, 2019; last reviewed April 16, 2019) (page 1 of 2)

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<tr>
<th>Adverse Effects</th>
<th>Associated ARVs</th>
<th>Onset/ Clinical Manifestations</th>
<th>Estimated Frequency</th>
<th>Risk Factors</th>
<th>Prevention/ Monitoring</th>
<th>Management</th>
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<tbody>
<tr>
<td>Anemia*</td>
<td>ZDV</td>
<td>Onset: • Variable, weeks to months Presentation Most Commonly: • Asymptomatic • Mild fatigue • Pallor • Tachypnea Rarely: • Congestive heart failure</td>
<td>Newborns Exposed to HIV: • Severe anemia is uncommon but may be seen coincident with physiologic Hgb nadir. Children with HIV Who Are Taking ARV Drugs: • Anemia is two to three times more common with ZDV-containing regimens compared to all other regimens.</td>
<td>Newborns Exposed to HIV: • Premature birth • In utero exposure to ZDV-containing regimens • Advanced maternal HIV • Neonatal blood loss • Combination ARV prophylaxis or empiric HIV therapy, particularly with ZDV plus 3TC Children with HIV Who Are Taking ARV Drugs: • Underlying hemoglobinopathy (e.g., sickle cell disease, G6PD deficiency) • Myelosuppressive drugs (e.g., TMP-SMX, rifabutin) • Iron deficiency • Advanced or poorly controlled HIV disease • OIs of the bone marrow • Malnutrition</td>
<td>Newborns Exposed to HIV: • Obtain CBC at birth. • Consider repeating CBC at 4 weeks for neonates who are at higher risk (e.g., those born prematurely or who are known to have low birth Hgb) and for neonates who receive ZDV beyond 4 weeks. Children with HIV Who Are Taking ARV Drugs: • Avoid ZDV in children with severe anemia when alternative agents are available. • Obtain CBC as part of routine care (see Clinical and Laboratory Monitoring of Pediatric HIV Infection).</td>
<td>Newborns Exposed to HIV: • Anemia rarely requires intervention unless Hgb is &lt;7.0 g/dL or is associated with symptoms. • ZDV administration can be limited to 4 weeks in low-risk neonates (see Antiretroviral Management of Newborns with Perinatal HIV Exposure or Perinatal HIV). Children with HIV Who Are Taking ARV Drugs: • Discontinue non-ARV, marrow-toxic drugs, if feasible. • Treat coexisting iron deficiency, OIs, and malignancies. • For persistent, severe anemia that is thought to be associated with ARV drugs (typically macrocytic anemia), switch to a regimen that does not contain ZDV.</td>
</tr>
<tr>
<td>Macrocytosis</td>
<td>ZDV</td>
<td>Onset: • Within days to weeks of starting therapy Presentation: • Asymptomatic but MCV is often &gt;100 fl • Sometimes associated with anemia</td>
<td>All Ages: • &gt;90% to 95%</td>
<td>None</td>
<td>No monitoring required—macrocytosis can be detected if CBC is obtained as part of routine care (see Clinical and Laboratory Monitoring of Pediatric HIV Infection).</td>
<td>No management required.</td>
</tr>
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</table>
### Key to Acronyms:
- **3TC** = lamivudine
- **ANC** = absolute neutrophil count
- **ARV** = antiretroviral
- **CBC** = complete blood count
- **dL** = deciliter
- **fL** = femtoliter
- **G6PD** = glucose-6-phosphate dehydrogenase
- **Hgb** = hemoglobin
- **MCV** = mean cell volume
- **NRTI** = nucleoside reverse transcriptase inhibitor
- **OI** = opportunistic infection
- **TMP-SMX** = trimethoprim-sulfamethoxazole
- **ZDV** = zidovudine

### Table 15d. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Hematologic Effects

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<td>Neutropeniaa</td>
<td>ZDV</td>
<td>Onset: Variable Presentation: Asymptomatic</td>
<td>Newborns Exposed to HIV: Rare Children with HIV Who Are Taking ARV Drugs: 2% to 4% of children on ARV drugs Highest rates occur in children on ZDV-containing regimens</td>
<td>Newborns Exposed to HIV: In utero exposure to ARV drugs Combination ARV prophylaxis, particularly with ZDV plus 3TC Children with HIV Who Are Taking ARV Drugs: Advanced or poorly controlled HIV infection Myelosuppressive drugs (e.g., TMP-SMX, ganciclovir, hydroxyurea, rifabutin)</td>
<td>Children with HIV Who Are Taking ARV Drugs: Obtain CBC as part of routine care.</td>
<td>Newborns Exposed to HIV: No established threshold for intervention; some experts would consider using an alternative NRTI for prophylaxis if ANC reaches &lt;500 cells/mm³. ZDV administration can be limited to 4 weeks in low-risk neonates (see Antiretroviral Management of Newborns with Perinatal HIV Exposure or Perinatal HIV). Children with HIV Who Are Taking ARV Drugs: Discontinue non-ARV, marrow-toxic drugs, if feasible. Treat coexisting OIs and malignancies. For persistent, severe neutropenia that is thought to be associated with ARV drugs, change to a regimen that does not contain ZDV.</td>
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**a** HIV infection itself, OIs, and medications used to prevent OIs (e.g., TMP-SMX) may all contribute to anemia and neutropenia.

**References**


