Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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<table>
<thead>
<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>
</tr>
</thead>
<tbody>
<tr>
<td>Lipodystrophy (Fat Maldistribution)</td>
<td>General Information</td>
<td>See below for specific associations.</td>
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<td></td>
<td></td>
<td>Onset:</td>
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<td>Prevention:</td>
<td>Physicians should perform a regimen review and consider changing the regimen when lipodystrophy occurs.</td>
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<td></td>
<td></td>
<td>• Increase in trunk and limb fat are the first sign; peripheral fat wasting may not appear for 12–24 months after ART initiation.</td>
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<td>Initiate a calorically appropriate, low-fat diet and an exercise regimen.</td>
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<td></td>
<td>Frequency is low (&lt;5%) with current regimens.</td>
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<td>Monitoring:</td>
<td>Improvement in fat maldistribution can vary following a regimen change. Improvement may occur after several months or years, or it may not occur at all.</td>
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<td></td>
<td></td>
<td>Genetic predisposition</td>
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<td>Puberty</td>
<td>• BMI measurement</td>
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<td></td>
<td></td>
<td>HIV-associated inflammation</td>
<td></td>
<td>Older age</td>
<td>• Waist circumference and waist-hip ratio</td>
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<td></td>
<td></td>
<td>Obesity before initiation of therapy</td>
<td></td>
<td>Longer duration of ART</td>
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<td></td>
<td></td>
<td>Body habitus</td>
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<td>Body habitus</td>
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<tr>
<td>Central Lipohypertrophy or Lipo-accumulation</td>
<td>Can occur in the absence of ART, but these conditions are most often associated with the use of PIs and EFV.</td>
<td>Presentation:</td>
<td></td>
<td>Obesity before initiation of ART</td>
<td>Prevention:</td>
<td>Counsel patient on lifestyle modification and dietary interventions (e.g., maintaining a calorically appropriate diet that is low in saturated fats and simple carbohydrates, and starting an exercise regimen, especially strength training).</td>
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<td>• Central fat accumulation with increased abdominal girth, which may include a dorsocervical fat pad (buffalo hump). Gynecomastia may occur in males or breast hypertrophy may occur in females, particularly with the use of EFV.</td>
<td></td>
<td>Sedentary lifestyle</td>
<td>Initiate a calorically appropriate, low-fat diet and an exercise regimen.</td>
<td>Recommend smoking cessation (if applicable) to decrease future CVD risk.</td>
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<td></td>
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<td>Frequency is low (&lt;5%) with current regimens.</td>
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<td>Monitoring:</td>
<td>Consider using an INSTI instead of a PI or EFV, although some INSTIs may be associated with generalized weight gain (see below).</td>
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<tr>
<td></td>
<td></td>
<td>Obesity before initiation of therapy</td>
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<td></td>
<td>Sedentary lifestyle</td>
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**Data are Insufficient to Allow the Panel to Safely Recommend Use of Any of the Following Modalities in Children:**
- Recombinant human growth hormone
- Growth hormone-releasing hormone
- Metformin
- Thiazolidinediones
- Recombinant human leptin
- Anabolic steroids
- Liposuction
Table 15h. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Lipodystrophies and Weight Gain  (Last updated April 14, 2020; last reviewed April 14, 2020)  (page 2 of 2)

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<td>Facial/Peripheral Lipoatrophy</td>
<td>Most cases are associated with the use of ZDV, a thymidine analogue NRTI.</td>
<td>Presentation: • Thinning of subcutaneous fat in the face, buttocks, and extremities, measured as a decrease in trunk/limb fat by DXA or triceps skinfold thickness. Preservation of lean body mass distinguishes lipoatrophy from HIV-associated wasting.</td>
<td>Frequency is low (&lt;5%) with current regimens.</td>
<td>Underweight before ART initiation</td>
<td>Prevention: • Limit the use of ZDV. Monitoring: • Patient self-report and physical examination are the most sensitive methods of monitoring lipoatrophy.</td>
<td>Replace ZDV with another NRTI when possible. Data are Insufficient to Allow the Panel to Safely Recommend Use of Any of the Following Modalities in Children: • Injections of poly-L-lactic acid • Recombinant human leptin • Autologous fat transplantation • Thiazolidinediones</td>
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<tr>
<td>Weight Gain</td>
<td>Significant weight gain may occur with all ARV regimens, but it appears to be more pronounced with DTG, BIC, and TAF.</td>
<td>Gradual weight gain after initiating ARV drugs is common with all currently used regimens. The mechanism for weight gain is unclear and is under investigation.</td>
<td>Rate of development of obesity is unclear.</td>
<td>In Adults: • Low pre-treatment BMI • Older age • Female sex • Black race Risk factors for weight gain have not yet been evaluated in infants and children.</td>
<td>Prevention: • Initiate a calorically appropriate, low-fat diet and an exercise regimen. Monitoring: • BMI measurement • Waist circumference and waist-hip ratio</td>
<td>Counsel patient on lifestyle modification and dietary interventions (e.g., maintaining a calorically appropriate, healthy diet that is low in saturated fats and simple carbohydrates, and starting an exercise regimen, especially strength training).</td>
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Key: ART = antiretroviral therapy; ARV = antiretroviral; BIC = bictegravir; BMI = body mass index; CVD = cardiovascular disease; DTG = dolutegravir; DXA = dual energy x-ray absorptiometry; EFV = efavirenz; INSTI = integrase strand transfer inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; TAF = tenofovir alafenamide; ZDV = zidovudine

References

See the archived version of Supplement III, February 23, 2009, Pediatric Guidelines on the AIDSinfo website for a more complete discussion and reference list.

General Reviews


2. Alves Junior CAS, de Lima LRA, de Souza MC, Silva DAS. Anthropometric measures associated with fat mass estimation in children and adolescents with HIV.


Associated ARVs/Etiology


16. McComsey GA, Libutti DE, O’Riordan M, et al. Mitochondrial RNA and DNA alterations in HIV lipoatrophy are linked to antiretroviral therapy and not to HIV.
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Management


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