Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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Table 15f. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Insulin Resistance, Asymptomatic Hyperglycemia, Diabetes Mellitus  *(Last updated April 27, 2017; last reviewed April 27, 2017)*

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<th>Adverse Effects</th>
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<th>Onset/Clinical Manifestations</th>
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</table>
| Insulin Resistance, Asymptomatic Hyperglycemia, DM<sup>a</sup> | ZDV, d4T, ddI, LPV/r, IDV, Rarely other PIs | Onset: Weeks to months after beginning therapy  
Presentation:  
• Asymptomatic fasting hyperglycemia (possibly in the setting of lipodystrophy), metabolic syndrome, or growth delay  
• Symptomatic DM (rare) | Insulin Resistance  
ARV-Treated Children:  
• 6% to 12%  
Impaired Fasting Glucose  
ARV-Treated Children:  
• 0% to 7%  
Impaired Glucose Tolerance  
ARV-Treated Children:  
• 3% to 4%  
DM  
ARV-Treated Children:  
• 0.2 per 100-person-years | Risk Factors for Type 2 DM:  
• Lipodystrophy  
• Metabolic syndrome  
• Family history of DM  
• High BMI (obesity) | Prevention:  
• Lifestyle modification  
• Avoid ZDV, d4T, ddI when possible. | Counsel on lifestyle modification (e.g., a diet low in saturated fat, cholesterol, transfat, and refined sugars; increased physical activity; cessation of smoking); consultation with dietician. |
|                |                 |                              |                     |             | Monitoring:  
• Monitor for signs of DM, change in body habitus, acanthosis nigricans. | Change NRTI backbone (e.g., from ZDV, d4T, or ddI to TAF, TDF, or ABC). |
|                |                 |                              |                     |             | Obtain RPG Levels at:  
• Initiation of ARV therapy  
• 3–6 months after therapy initiation  
• Once a year thereafter | For Either RPG ≥200 mg/dL plus Symptoms of DM or FPG ≥126 mg/dL:  
• Patient meets diagnostic criteria for DM; consult endocrinologist. |
|                |                 |                              |                     |             | For RPG ≥140 mg/dL:  
• Obtain FPG performed after 8-hour fast and consider referral to endocrinologist. | FPG 100–125 mg/dL:  
Impaired FPG is suggestive of insulin resistance; consult endocrinologist. |
|                |                 |                              |                     |             | FPG <100 mg/dL:  
Normal FPG, but Does Not Exclude Insulin Resistance:  
• Recheck FPG in 6–12 months. | |

<sup>a</sup> Insulin resistance, asymptomatic hyperglycemia, and DM form a spectrum of increasing severity. *Insulin resistance* is often defined as elevated insulin levels for the level of glucose observed; *impaired FPG* as an FPG of 100–125 mg/dL; *impaired glucose tolerance* as an elevated 2-hour PG of 140–199 mg/dL in a 75 g OGTT (or if <43 kg, 1.75 g/kg of glucose up to a maximum of 75 g); and *diabetes mellitus* as either an FPG ≥126 mg/dL, a random PG ≥200 mg/dL in a patient with hyperglycemia symptoms, an HgbA1C of ≥6.5%, or a 2-hour PG after OGTT ≥200 mg/dL. However, the Panel does not recommend routine determinations of insulin levels, HgbA1C, or glucose tolerance without consultation with an endocrinologist; these guidelines are instead based on the readily available random and fasting plasma glucose levels.

**Key to Acronyms:**  
ABC = abacavir; ARV = antiretroviral; BMI = body mass index; d4T = stavudine; ddI = didanosine; dL = deciliter; DM = diabetes mellitus; FPG = fasting plasma glucose; HgbA1c = glycosylated hemoglobin; IDV = indinavir; LPV/r = lopinavir/ritonavir; NRTI = nucleoside reverse transcriptase inhibitor; OGTT = oral glucose tolerance test; PG = plasma glucose; PI = protease inhibitor; RPG = random plasma glucose; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; ZDV = zidovudine

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References


