### Table 13f. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Insulin Resistance, Asymptomatic Hyperglycemia, Diabetes Mellitus  
*(Last updated April 27, 2017; last reviewed April 27, 2017)*

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


