Table 17f. Antiretroviral Therapy–Associated Adverse Effects and Management Recommendations—Insulin Resistance, Asymptomatic Hyperglycemia, and Diabetes Mellitus

Updated: September 30, 2025
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Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
Insulin Resistance, Asymptomatic Hyperglycemia, and Diabetes Mellitus[a]	ZDV, LPV/r, and possibly other PIs and INSTIs	**Onset** • Weeks to months after beginning therapy **Presentation** • Asymptomatic fasting hyperglycemia (which sometimes occurs in the setting of lipodystrophy), metabolic syndrome, or growth delay • Symptomatic DM (rare)	**Children** • IR, 6% to 12% (incidence is higher during puberty, 20% to 30%) • IFPG, 0% to 7% • IGT, 3% to 4% • DM, 0.2 per 100 child-years	**Risk Factors for Type 2 DM** • Lipodystrophy • Metabolic syndrome • Family history of DM • High BMI (obesity)	**Prevention** • Lifestyle modification **Monitoring** • Monitor for signs of DM, change in body habitus, and acanthosis nigricans. • Obtain RPG levels at initiation of ART, 3–6 months after ART initiation, and yearly thereafter. • In patients with an RPG ≥140 mg/dL, obtain FPG after an 8-hour fast and consider referring the patient to an endocrinologist.	Counsel patient on lifestyle modification (e.g., implementing a diet low in saturated fat, cholesterol, trans fat, and refined sugars; increasing physical activity; ceasing smoking). Recommend that the patient consult with a dietician. If the patient is receiving ZDV, switch to TAF, TDF, or ABC. **For Patients With Either an RPG ≥200 mg/dL Plus Symptoms of DM or an FPG ≥126 mg/dL** • These patients meet diagnostic criteria for DM; consult an endocrinologist.

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						For Patients With an FPG of 100–125 mg/dL • Impaired FPG suggests insulin resistance; consult an endocrinologist. **For Patients With an FPG of <100 mg/dL** • This FPG is normal, but a normal FPG does not exclude IR. Recheck FPG in 6–12 months.

[a] IR, asymptomatic hyperglycemia, IFPG, IGT, and DM form a spectrum of increasing severity.

IR: Often defined as elevated insulin levels for the level of glucose observed.
IFPG: Often defined as an FPG of 100–125 mg/dL.
IGT: Often defined as an elevated 2-hour plasma glucose (PG) of 140–199 mg/dL in a 75-g oral glucose tolerance test (OGTT) (or, if the patient weighs <43 kg, 1.75 g per kg of glucose up to a maximum of 75 g).
DM: Often defined as either an FPG ≥126 mg/dL, an RPG ≥200 mg/dL in a patient with hyperglycemia symptoms, a glycosylated hemoglobin (HgbA1c) of ≥6.5%, or a 2-hour PG ≥200 mg/dL in an OGTT.

However, the Panel on Antiretroviral Therapy and Medical Management of Children Living With HIV does not recommend performing routine measurements of insulin levels, HgbA1c, or glucose tolerance without consulting an endocrinologist. These guidelines are instead based on the readily available RPG and FPG levels. The HgbA1c test may underestimate glycemia in people with HIV; it is not recommended for diagnosis and may present challenges for monitoring.

Key: ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; BMI = body mass index; DM = diabetes mellitus; FPG = fasting plasma glucose; IFPG = impaired fasting plasma glucose; IGT = impaired glucose tolerance; INSTI = integrase strand transfer inhibitor; IR = insulin resistance; LPV/r = lopinavir/ritonavir; mg/dL = milligrams per deciliter; PI = protease inhibitor; RPG = random plasma glucose; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; ZDV = zidovudine

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