Insulin activates Na⁺-K⁺ ATPase pump, increases intracellular [K⁺], and promotes hypokalemia (event A).

Hyperglycemia (or fed state) promotes glycolysis, increases intracellular ATP/ADP ratio and closes the ATP-sensitive potassium channels. As a result of membrane depolarization gated calcium channels are opened and calcium moves into the cell and causes exocytosis of insulin-containing vesicles. Hence, hyperglycemia raises insulin (events B, C and D).

Sulfonylureas strongly close the ATP-sensitive potassium channels. They cause the same effect that is caused by high intracellular ATP/ADP ratio; that is, they promote insulin release. Therefore, sulfonylureas require a functional pancreas (events C and D).

Hypokalemia slows down the Na⁺-K⁺ ATPase pump, most likely, due to low extracellular concentration of potassium or low inward driving force for potassium. As a result insulin secretion is decreased. The latter causes hyperglycemia (event E).

Hyperkalemia conversely speeds up the Na⁺-K⁺ ATPase pump due to high extracellular concentration of potassium or high inward driving force for potassium, and increases the insulin secretion (event F).

Insulin-induced cellular uptake of potassium is independent of the enhanced uptake of glucose by insulin. Hence, diabetic patients are presented with moderate hyperkalemia that may proceed to serious hyperkalemic state if they receive a high potassium load.

Note on ECG Findings: Stimulation of Na⁺-K⁺ ATPase pump by insulin causes hyperpolarization of excitable cells and lengthens the repolarization phase. Hence, in type II diabetics that are presented with high levels of insulin, this may lead to increased Q-T interval, erratic beats and fainting spells.