This study examined the influence of both hydration and blood glucose concentration on cardiovascular drift during exercise, we first determined if the prevention of dehydration during exercise by full fluid replacement prevents the decline in stroke volume (SV) and cardiac output (CO) during prolonged exercise. On two occasions, 10 endurance-trained subjects cycled an ergometer in a 22°C room for 2 h, beginning at 70 ± 1% maximal O2 uptake (VO2max) and in a euhydrated state. During one trial, no fluid (NF) replacement was provided and the subject’s body weight declined 2.09 ± 0.19 kg or 2.9%. During the fluid replacement trial (FR), water was ingested at a rate that prevented body weight from declining after 2 h of exercise (i.e., 2.34 ± 0.17 ½ h). SV declined 15% and CO declined 7% during the 20- to 120-min period of the while heart rate (HR) increases 10 % and O2 uptake (VO2) increased 6% (all P < 0.05). In contrast, SV was maintained during the 20- to 120 min period of FR while HR increased 5% and thus CO actually increased 7% (all P < 0.05). Rectal temperature, SV, and HR were similar during the 1st h of exercise during NF and FR. However, after 2 h of exercise, rectal temperature was 0.6°C higher (P < 0.05) and SV and CO were 11-16% lower (P<0.05) during NF compared with FR. In another experiment using similar subjects (n=8) and exercise conditions, we observed that continuous intravenous infusion of glucose in water (1,224 ± 55 ml of 18% glucose, wt/vol) totally prevented the 5-7% increase (P<0.05) in Vo2, CO, and HR observed during 2 h of exercise when hydration was maintained by simply ingesting water. In conclusion, the maintenance of euhydration by fluid replacement throughout exercise attenuates hyperthermia and prevents the decline in SV and CO observed during the 2nd h exercise when no fluid is replaced. Additionally, when dehydration is offset during 2 h of cycle exercise performed at 70% Vo2max, it appears that factors that are influenced by hyperglycemic are responsible for the 5-7% increase in Vo2, HR, and CO and that these increases are prevented when both glucose and water are infused intravenously.