Numerous epidemiologic studies have now shown that insulin levels correlate with the development of cardiovascular disease after correction for other confounding variables. These findings leave open the possibility that excess circulating insulin is a risk factor that may have some predictive value in cardiovascular disease. Several years ago it was noted that low risk populations for ischemic heart disease have lower ambient insulin levels and insulin responses to glucose are higher in countries where the rate of ischemic heart disease is high (19,18). A number of large prospective studies where insulin levels were measured have now confirmed the relationship of insulin to cardiovascular disease. For example, in the Helsinki Policeman Study (13) those men in the highest quintile for fasting and post-glucose insulin levels had the highest incidence of ischemic heart disease, including myocardial infarction. Other studies such as the Busselton Study (22) in Australia and the Paris Civil Servants Study (5) have supported this relationship. In healthy, normotensive Italian factory workers, divided as having normal and high insulin levels, the hyperinsulinemic group had higher mean triglycerides and blood pressure and lower HDL cholesterol than the normoinsulinemic group (23). Thus, in the general population subjects with normal glucose tolerance and no evidence of diabetes, but with hyperinsulinemia, have an increased risk for ischemic heart disease and accompanying higher levels of other risk factors for ischemic cardiovascular disease.

Obesity and noninsulin-dependent diabetes mellitus (NIDDM) are associated with insulin resistance and hyperinsulinemia. Insulin resistance is a reduced sensitivity of insulin-mediated glucose disposal and is usually accompanied by compensatory increased secretion of insulin and hyperinsulinemia. In addition to obesity and NIDDM, it is now recognized that another common disorder, essential hypertension, is also accompanied by insulin resistance and hyperinsulinemia (14,4). In obese subjects plasma insulin responses to glucose are greater in hypertensive obese compared to normotensive obese (9). Ferrannini and coworkers (7) noted that insulin resistance could also be demonstrated in lean
essential hypertensive subjects with no other risk for insulin resistance. In these subjects insulin resistance was determined by insulin clamp techniques noting that stimulation of whole-body glucose uptake by insulin was reduced by 40% compared to controls. In addition, there was a direct relation of insulin resistance to level of blood pressure. In a larger study, Pollare, et al. (12) noted reduced insulin sensitivity in 143 hypertensive patients compared to 51 normotensive patients with a significant inverse correlation of insulin sensitivity to systolic blood pressure. Large prospective studies have also established an association between circulating insulin and blood pressure. Modan, et al. (11) reported in Israeli subjects a positive correlation of insulin and blood pressure independent of body weight. The San Antonio Heart Study examined metabolic and cardiovascular factors in 2,930 subjects from a bi-ethnic population noting that hypertension was present in 287 subjects (9.8% prevalence, [4,10])). Five other metabolic risk factors, including obesity, NIDDM, impaired glucose tolerance (IGT), high serum triglycerides and high total serum cholesterol were found with a much higher frequency in the hypertensive subjects. A positive correlation of insulin to diastolic blood pressure was found in the control normotensive population.

Several reports have not found an association of insulin and blood pressure or have noted only weak correlations (15). There appears to be significant ethnic differences in the association of insulin, insulin resistance and blood pressure. Pima Indians have a high incidence of obesity, insulin resistance and insulinemia, yet have a low prevalence of hypertension and there is no correlation between insulin resistance and mean arterial pressure compared to whites where a positive correlation is found (15). In young borderline hypertensive black males a reduced insulin sensitivity has been reported (6). However, other studies in normotensive adult blacks and in black children have not found a relation between insulin and blood pressure (15,21). Although there is a positive association of insulin and blood pressure in Mexican American men, the relation is weak when compared to non-Hispanic whites (4,10).

Insulin may increase blood pressure through effects on sodium transport, the sympathetic nervous system or through direct actions on the blood vessels (17). The infusion of insulin into normal subjects increases plasma norepinephrine and neural outflow suggesting the possibility that hyperinsulinemia could lead to a neurogenic hypertension (4). Acute insulin infusion also causes sodium retention by directly increasing tubular sodium reabsorption and could produce volume-dependent hypertension (4). Insulin has been shown in vitro to stimulate sodium transport