COMPETITIVE PROBLEMS IN THE DRUG INDUSTRY 13641

TABLE VIII

Regression of Incidence of Congestive Heart Failure on Diabetes: 18 Year Follow-Up Study

		Regression Coe	efficient	
	Men Aged 45 to 74 Years		Women Aged 45 to 74 Years	
	Bivariate*	Multivariate†	Bivariate*	Multivariatet
With Prior CHD or RHD‡ Coefficient t test§ (no. cases/no. at risk) Without Prior CHD or RHD∥	0.10 0.21 (59/1,700)	0.06 0.12 (58/1,641)	1.13 3.05 (49/1,323)	1.15 2.97 (47/1,275)
Coefficient t test (no. cases/no. at risk)	1.33 2.94 (38/12,407)	1.01 2.17 (36/11,899)	1.67 3.88 (37/16,936)	1.39 3.15 (37/16,160)

• The bivariate function was estimated by the method of Walker and Duncant using the variables diabetes and age.

† The multivariate function was estimated by the method of Walker and Duncan' using the variables diabetes and age, pressure, serum cholesterol and Framingham relative weight.

‡ To be included in this group at a given examination (n), the subject must have had coronary or rheumatic heart disease on or before examination (n + 1).

§ At test value of 1.96 is significant at the 0.05 level.

To be included in this group at a given examination (n), the subject must not have had coronary or rheumatic heart disease on or before examination (n + 1).

phate bonds to fuel the heart's work. It thus appears that glucose and insulin fuel the failing hypoxic heart.⁷⁻¹¹ This hypothesis would explain the difficulty of the diabetic ischemic heart but does not account for myocardial decompensation in the absence of

hypoxia.

However, in the diabetic heart there is some evidence to suggest that free fatty acids are also not used efficiently. Hearts of rats with alloxan-induced diabetes have been found to accumulate increased myocardial triglyceride in lipid droplets.⁸ Human di-abetic hearts extract more fatty acid and ketones than the nondiabetic heart, but in the light of the foregoing this phenomenon could indicate that more foregoing this phenomenon could indicate that more free fatty acid is being shunted into structural lipid as less is metabolized for energy. It may be that the diabetic heart, because of faulty utilization of fatty acid must, as in the case of ischemia, fall back on glycolytic metabolism for energy. This places it in jeop-ardy because the utilization of glucose, which is insu-lin-dependent, is also faulty. This energy crisis may be further compounded in the diabetic subject by a block between pyruvate and the tricarboxylic acid or Krebs cycle.

These major metabolic disturbances could provide These major metabolic disturbances could provide a metabolic basis for eventual myocardial failure. The fact that only the insulin-dependent diabetic patient appears peculiarly susceptible to congestive heart failure supports the foregoing in that only these diabetic patients appear to have difficulty with excessive and faulty acid metabolism leading to ketosis as well as impaired glycolysis. The fact that subjects with diabetes of adult onset treated by diet or orally administered drugs have no increased risk of congestive heart failure suggests that the central metabolic tive heart failure suggests that the central metabolic

TABLE IX

Regression of the Incidence of Congestive Heart Failure (Without Prior Coronary or Rheumatic Heart Disease*) on Treatment of Diabetes: 18 Year Follow-Up Study

Treatment	Bivariate Coefficient†	t Value	‡
Men Aged 45 to	o 74 Years		
Insulin	1.76	3.26	
Oral hypoglycemic agent	0.68	0.66	
Other	0.92	0.90	
Women Aged 45	to 74 Years		
Insulin	2.21	4.47	
Oral hypoglycemic agent	0.56	0.54	
Other	1.49	1.45	

* To be included in this group at a given examination (n), the subject must not have had coronary or rheumatic heart disease

on or before examination (n+1).
†The bivariate function was estimated by the method of Walker and Duncant using the variables type of diabetic treatment and age.

‡ At value of 1.96 is significant at the 0.05 level.

defect promoting failure may be ketosis and insulin deficiency. Once heart failure ensues, the process appears to be self-perpetuating since it has been shown that failure further suppresses insulin release. 10

Role of insulin-treated diabetes: The finding that the excess risk of congestive heart failure is considered to the insulin treated diabetic subjects or insuling the state of the insuling treated diabetic subjects or insuling the state of the insuling treated diabetic subjects or insulinsuling treated diabetic subjects or insuling treated diabetic su

fined to the insulin-treated diabetic subjects raises