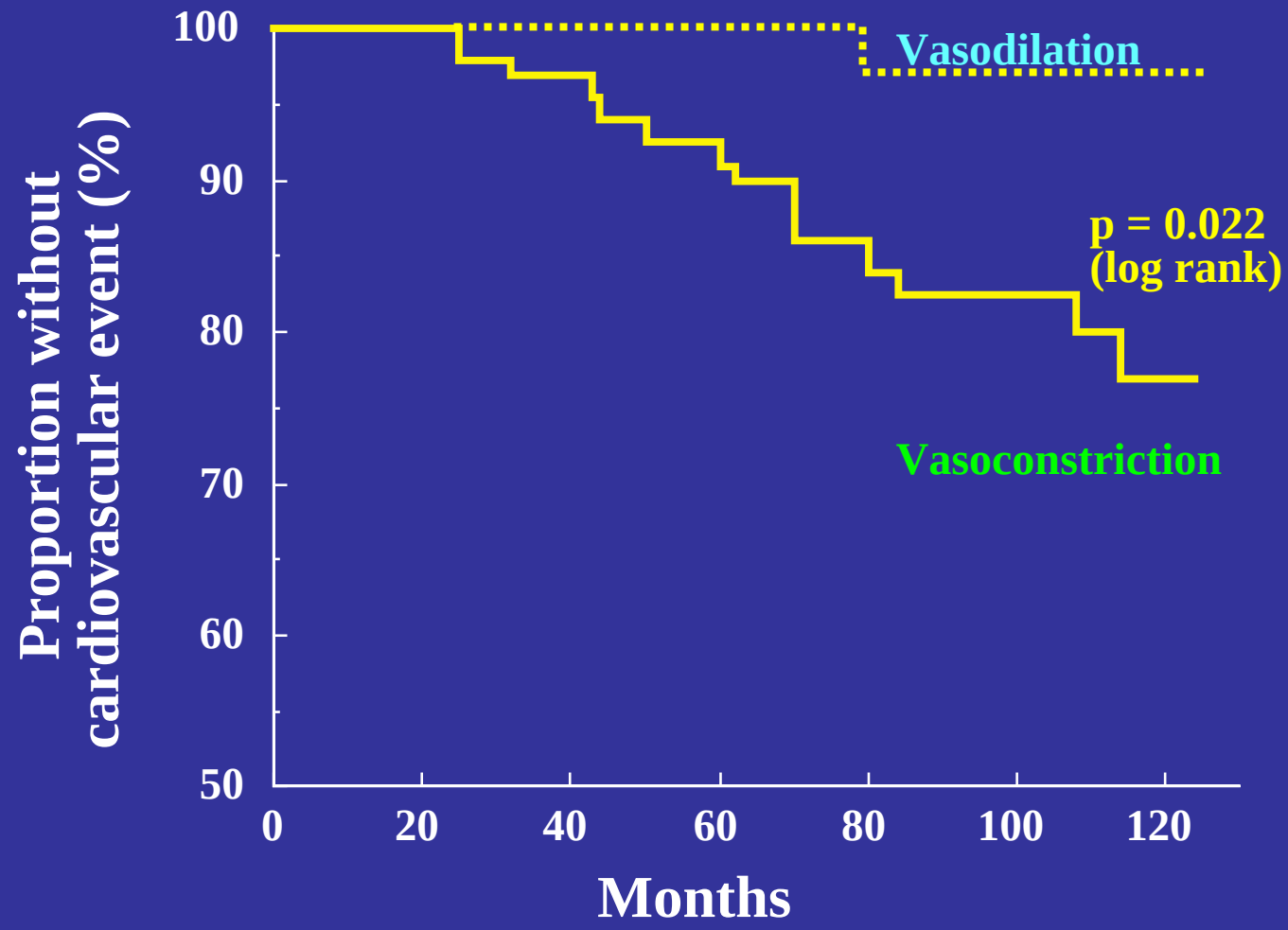
L-Carnitine and Endothelial Function

Helmut O. Steinberg, M.D.
Indiana University Medical School
Indianapolis, IN

Introduction

- Endothelium participates in the regulation of vascular tone, thrombosis, and VSMC proliferation and migration
- Increased rates of cardiovascular mortality and morbidity in obesity and type 2 DM
- Endothelial function is impaired in obesity and type 2 diabetes
- Impaired endothelial function is a predictor of CVD

Acetylcholine-Induced Vasoreactivity as a Predictor of Cardiovascular Events



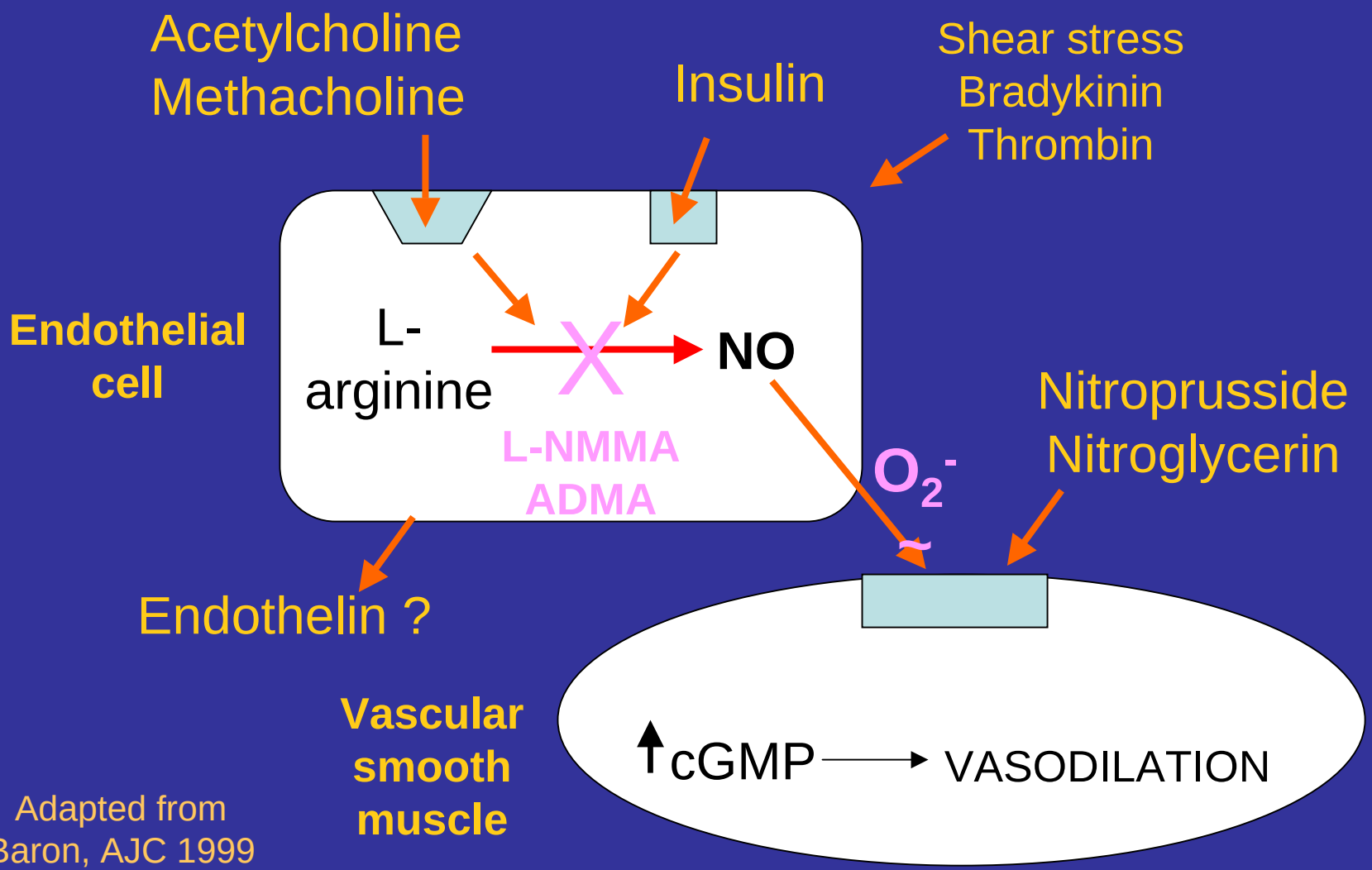
number exposed to risk:							
Vasodilation:	50	39	37	36	24	17	7
Vasoconstriction:	95	83	70	64	50	35	12

Schachinger, et al. Circulation. 2000; 101:pg 1902.

Introduction cont.

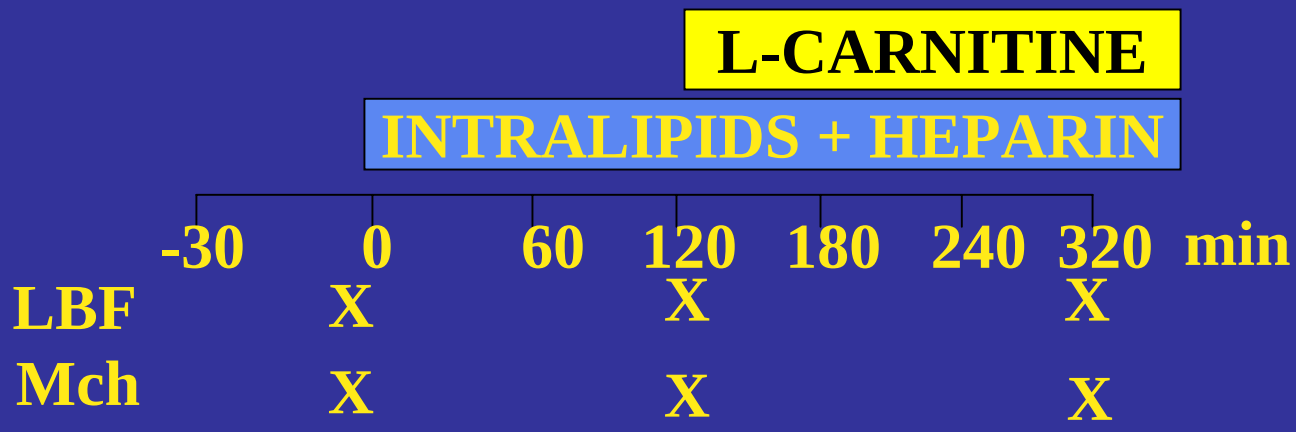
- FFA levels are elevated in obesity and DM
- Carnitine levels have been reported to be decreased in DM
- Carnitine supplementation has been reported to improve vascular function

Endothelial nitric oxide system



Adapted from Baron, AJC 1999

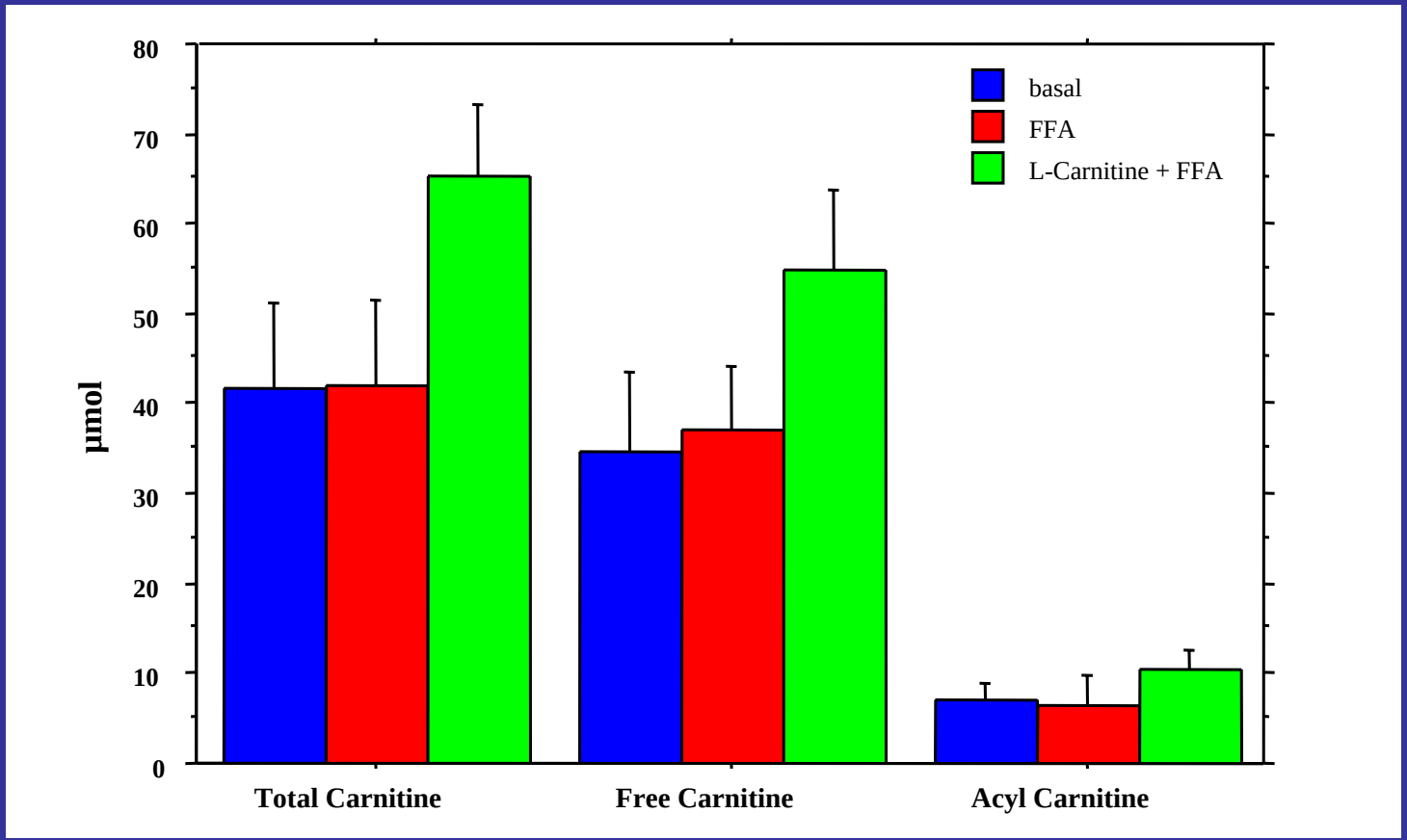
Protocol 1
Effect of L-Carnitine on FFA induced endothelial dysfunction



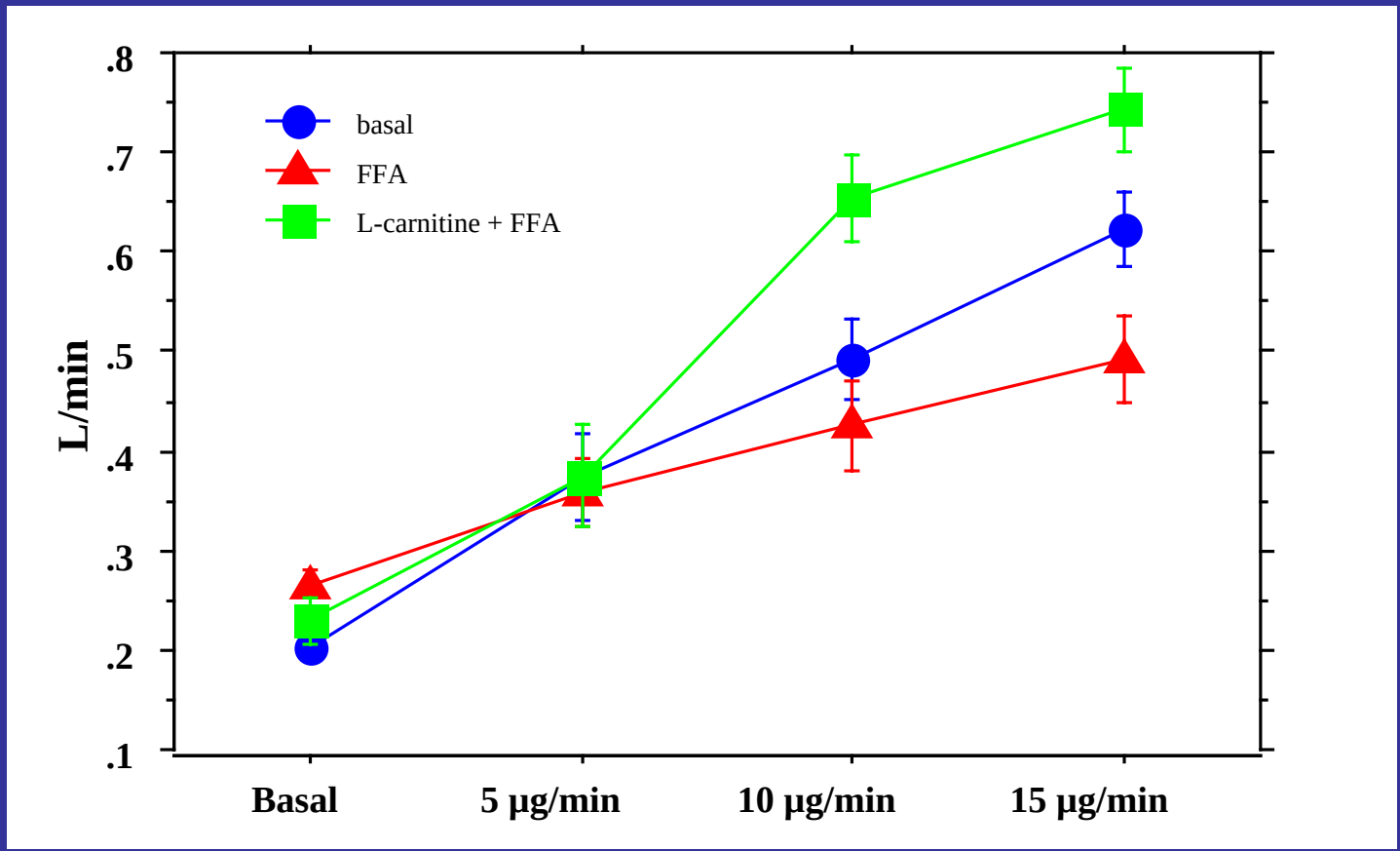
Demographic, Metabolic, and Hemodynamic Variables

Age (years)	**32±5**
Body Mass Index	**22±2**
% body fat	**17±3**
Glucose (mg/dl)	**93±2**
Total Cholesterol (mg/dl)	**147±9**
Triglycerides (mg/dl)	**71±11**
HDL-Cholesterol (mg/dl)	**45±6**
LDL-Cholesterol (mg/dl)	**88±6**
MAP (mmHg)	**94±5**
Heart Rate (bpm)	**62±3**

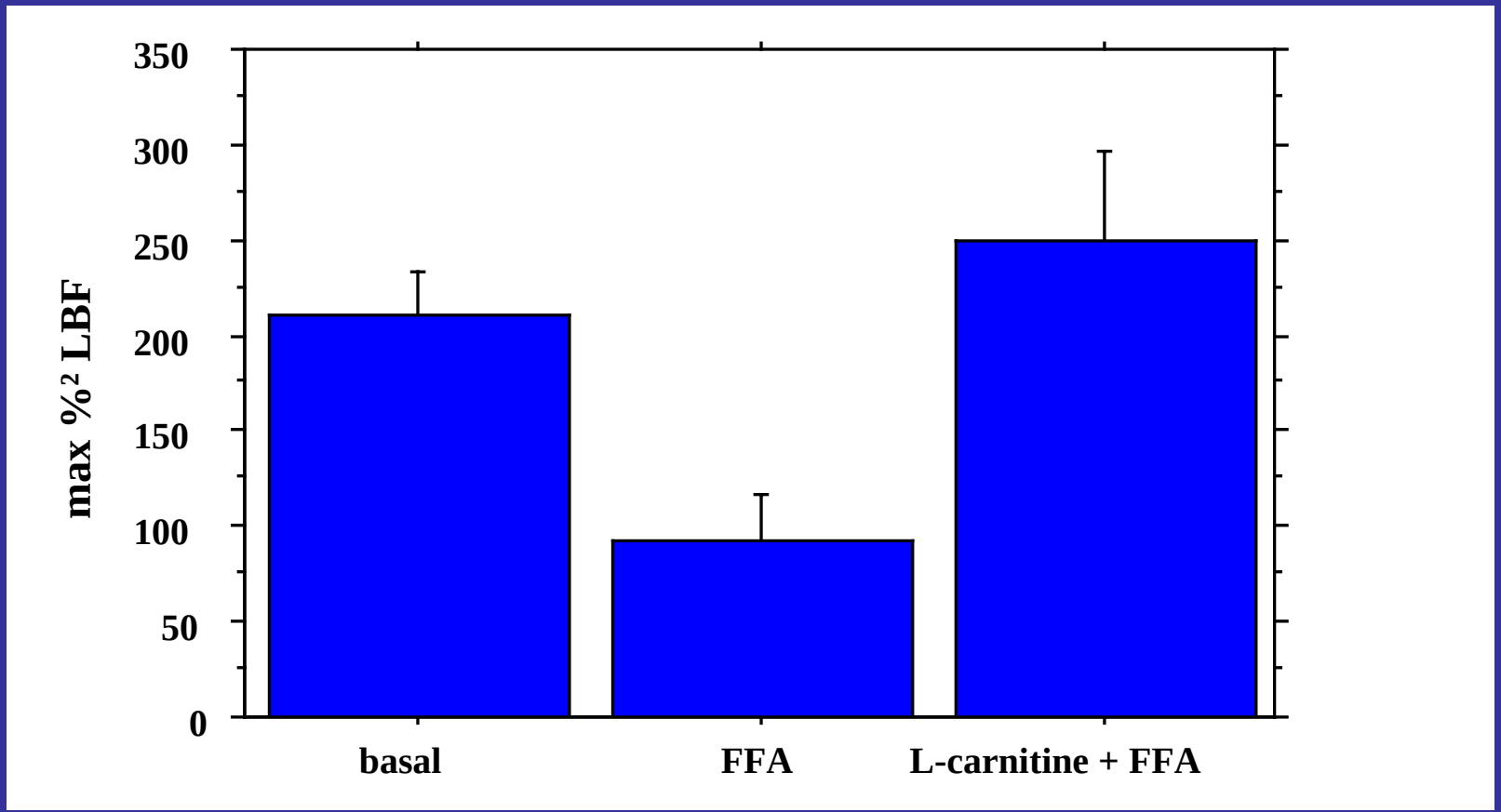
Carnitine Levels



LBF in response to Methacholine

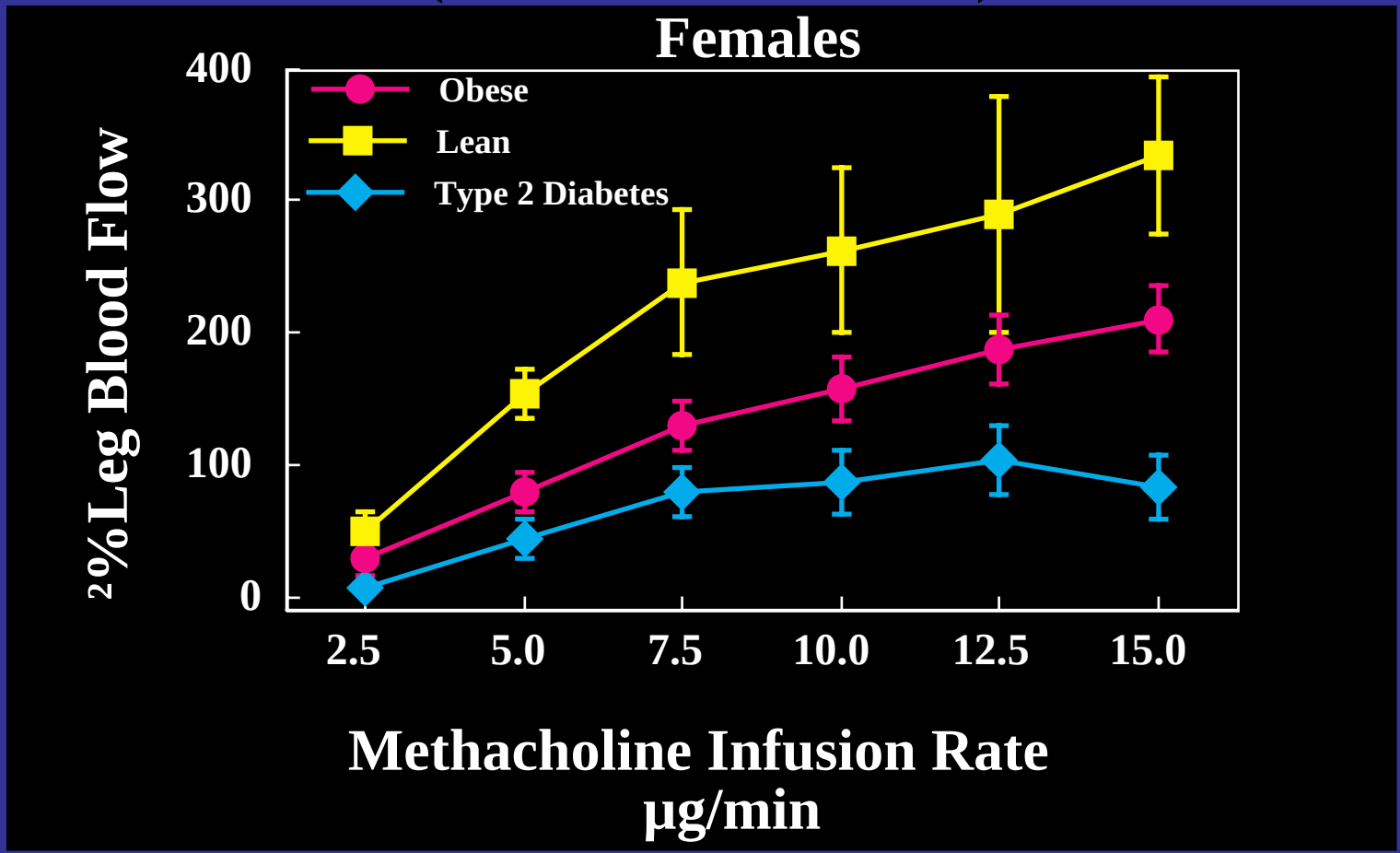


Maximal change in LBF in response to Methacholine



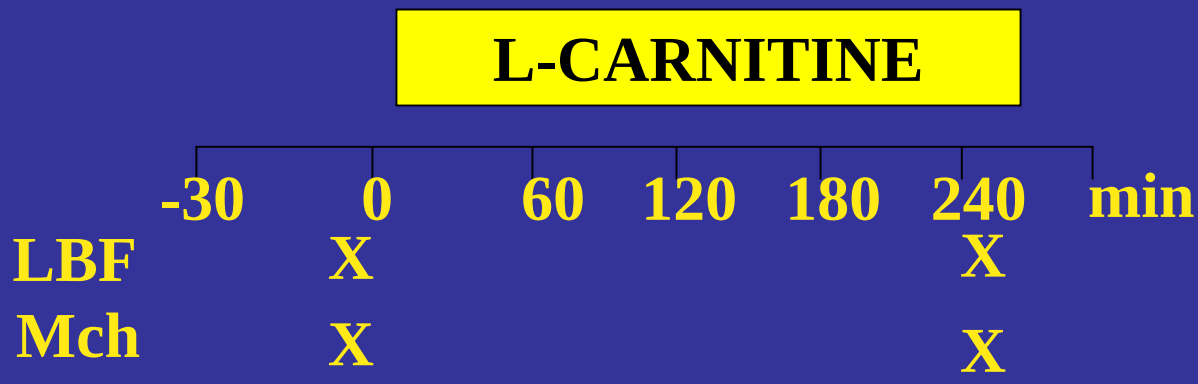
Effect of Body Fat and Type 2 Diabetes on Endothelial Dependent Vasodilation

(Endothelial Function)



Protocol 2

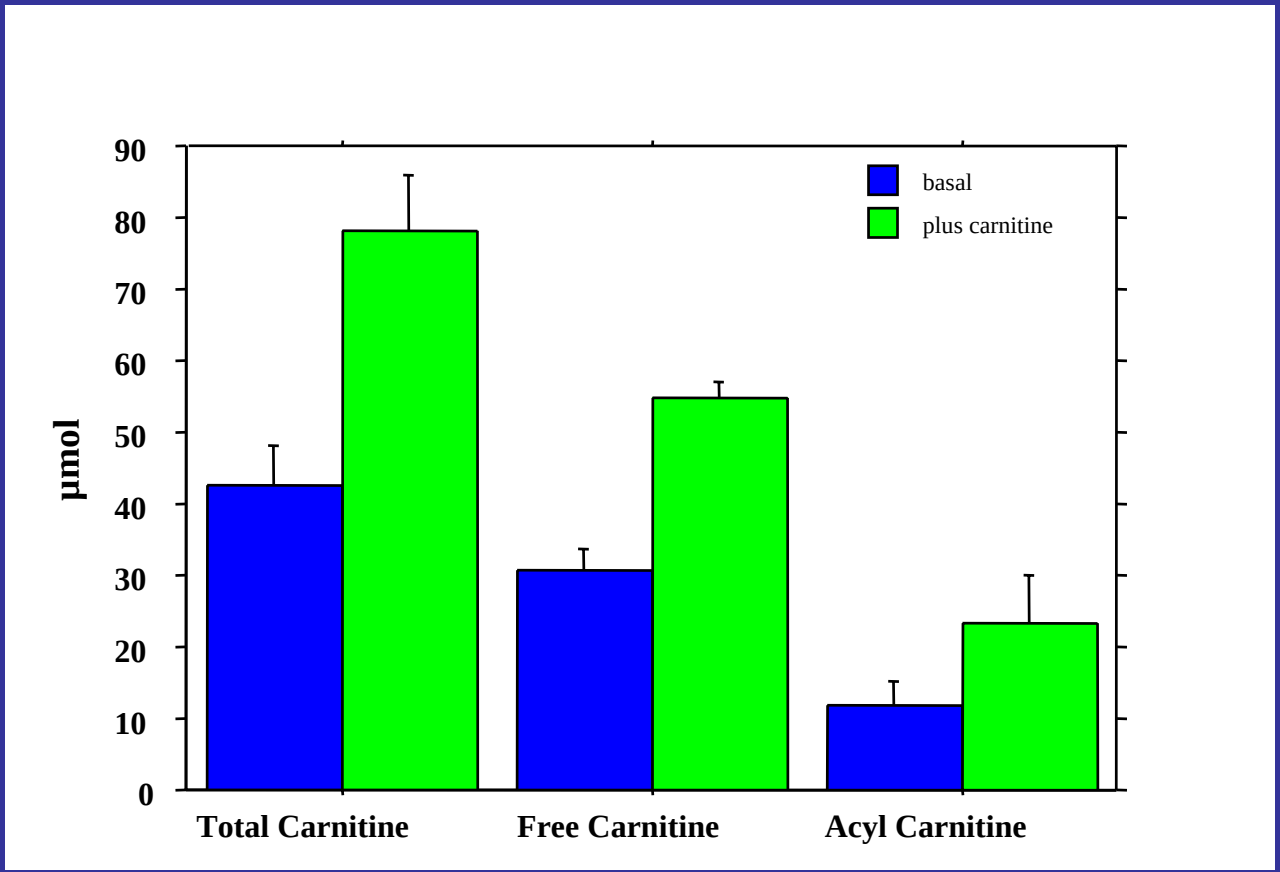
Effect of L-Carnitine on endothelial function in obese subjects



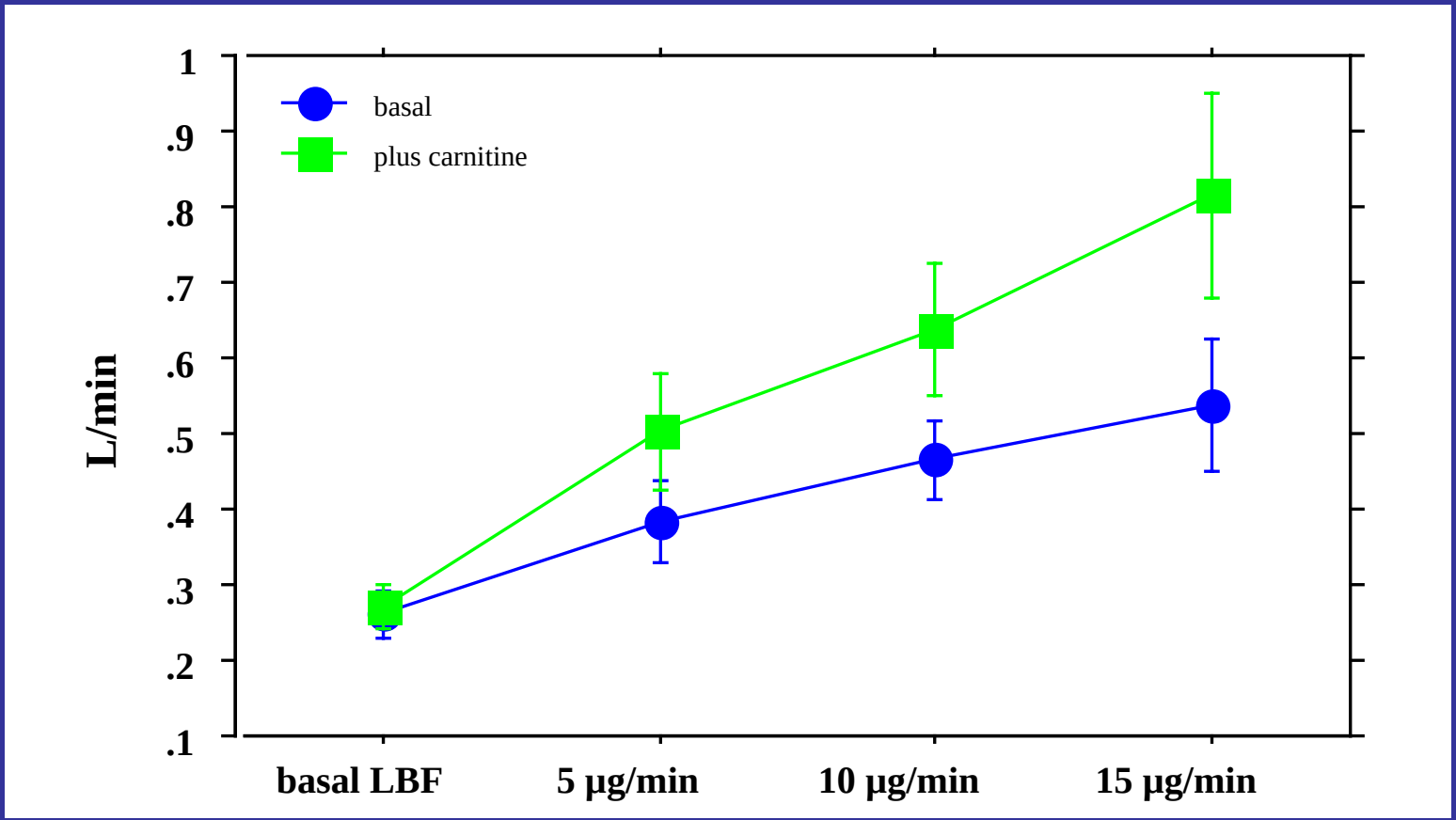
Demographic, Metabolic, and Hemodynamic Variables

Age (years)	35±4
Body Mass Index	32±3
% body fat	42±3
Glucose (mg/dl)	93±3
Total Cholesterol (mg/dl)	179±10
Triglycerides (mg/dl)	115±19
HDL-Cholesterol (mg/dl)	41±3
LDL-Cholesterol (mg/dl)	116±9
MAP (mmHg)	100±5
Heart Rate (bpm)	65±4

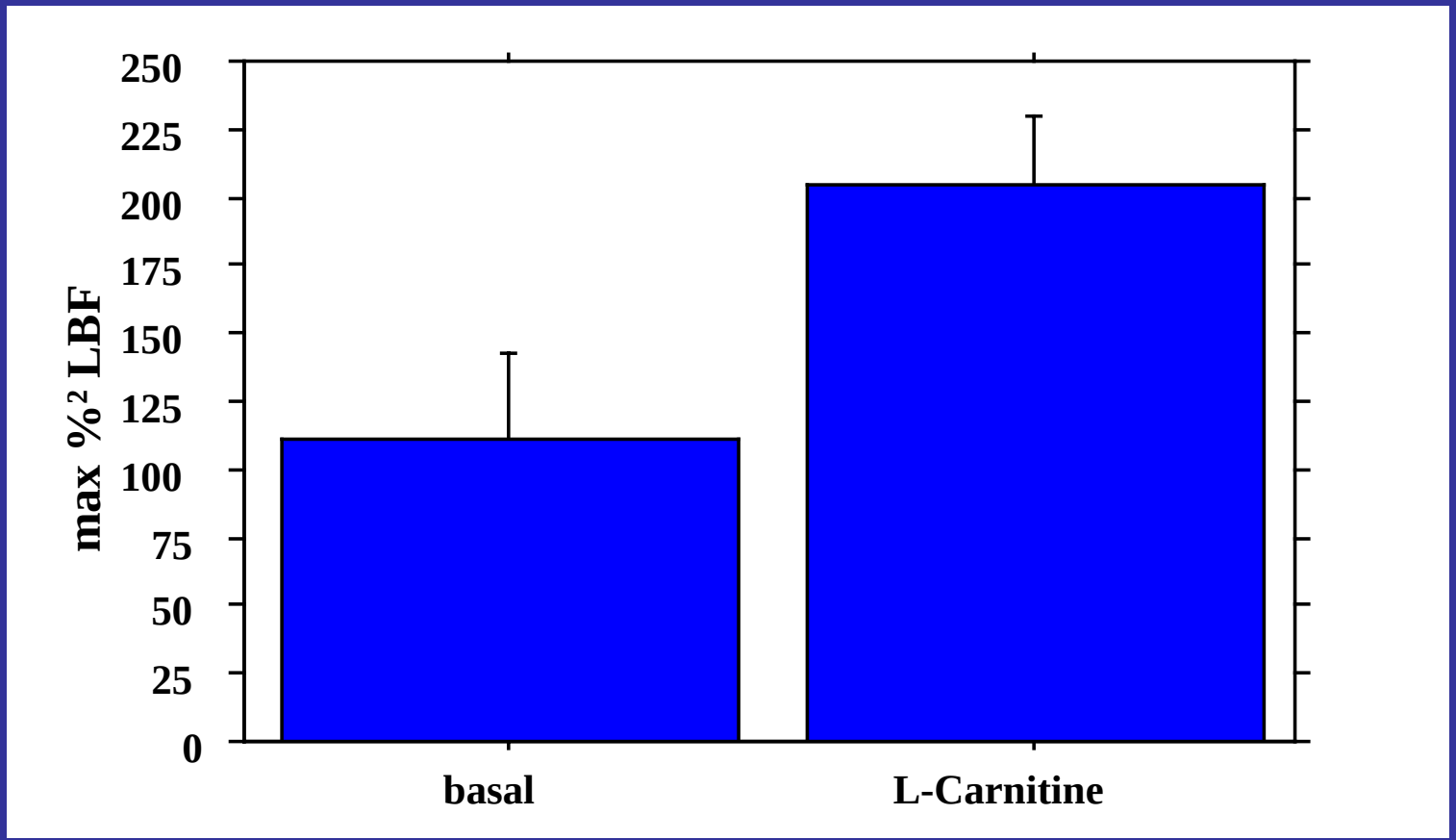
Carnitine Levels



LBF in response to Methacholine



Maximal change in LBF in response to Methacholine



Summary and Conclusion

- In the lean group FFA elevation caused a fall in Acyl-carnitine levels and blunting of LBF responses to Mch. Administration of L-carnitine restored both, acyl-carnitine levels and the normal LBF response to Mch.
- In the obese group, LBF responses to Mch were blunted under basal conditions. 4 hour infusion of L-carnitine increased acyl- L-canitine levels and improved the LBF response to Mch.
- Our data suggest that short term elevation of FFA depletes the systemic acyl-carnitine pool. This could be due to a direct effect of FFA, a decreased production, or a shift of acyl-carnitine into cells.
- The results of our studies indicate that administration of L-carnitine may exert protective effects on the vasculature. This effect appears to be mediated at least in part via the improved release or action of nitric oxide. Further work is necessary to characterize the mechanism(s) by which L-carnitine improves vascular function.

Further Research

- **Define cellular mechanism of L-carnitine action on endothelial function.**
- **Assess effect of oral L-carnitine supplements on vascular function in type 2 DM and obesity.**

These Studies would not be possible without

- **Collaborators:**
  Sudha S.Shankar, M.D.
  Bahram Mirzamohammadi, M.D.
  James P. Walsh, M.D.
- **Research volunteers**
- **GCRC support**