

# **II° Convegno Nazionale del Centro Studi AMD**

**16/10/04 LUGGIA**

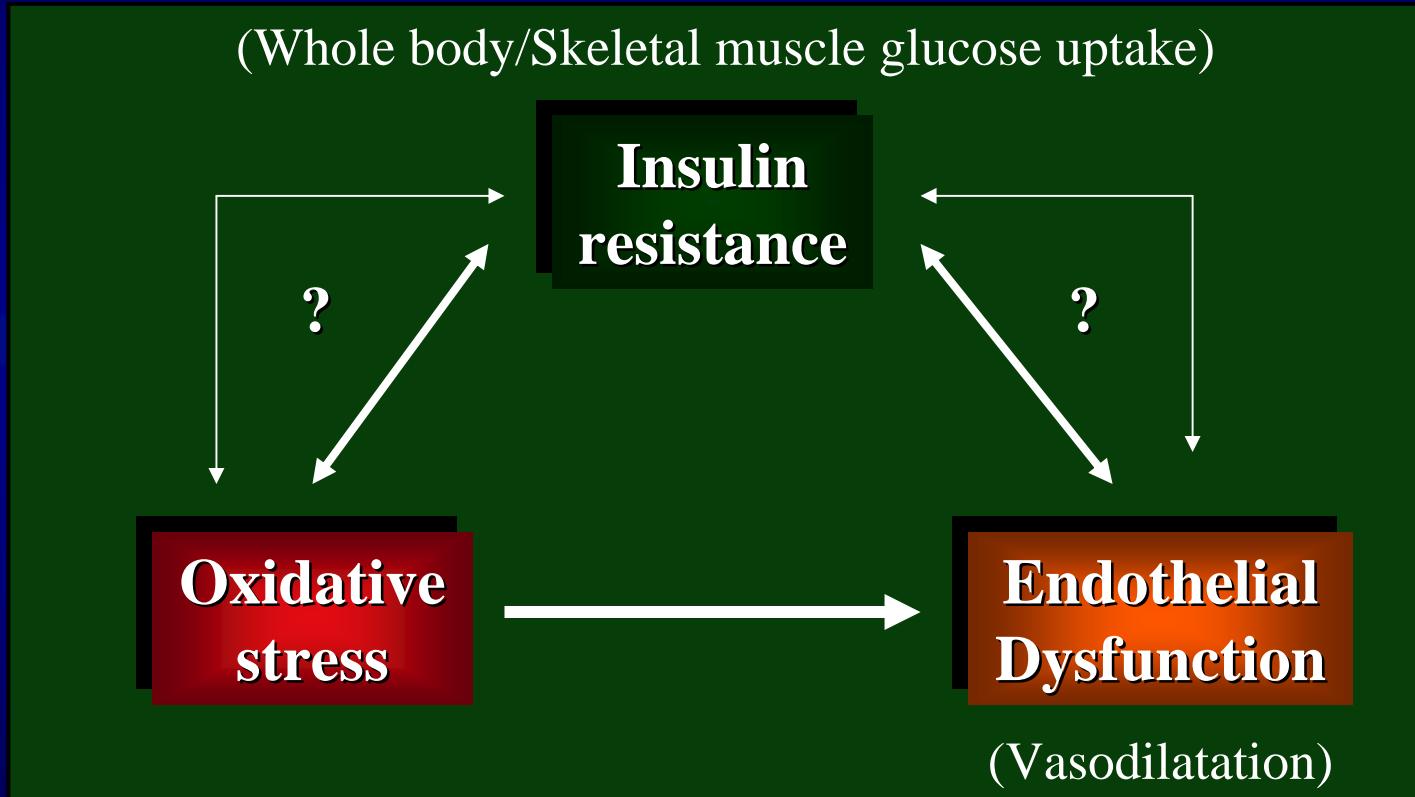
**L'endotelio, la resistenza insulinica e lo  
stress ossidativo, dalla fisiopatologia  
all'applicazione clinica**



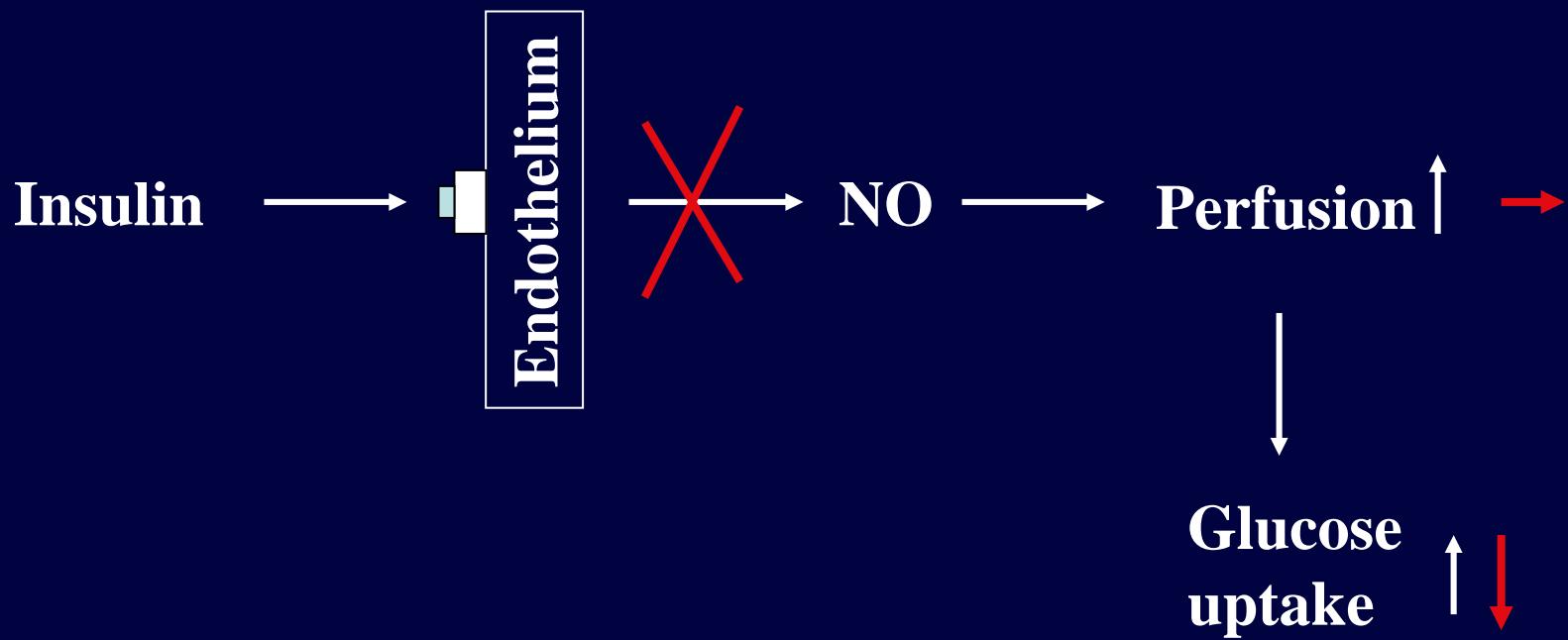
**Andrea Natali**  
*Dipartimento di Medicina Interna*  
Università di Pisa



# ***IR, Oxidative Stress and ED***



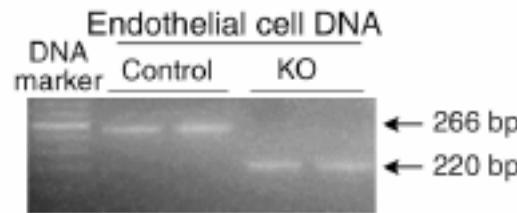
# Hypothesis (1): ED $\rightarrow$ IR



# Vasc. ENdoth. Ins. Recep. K.O.

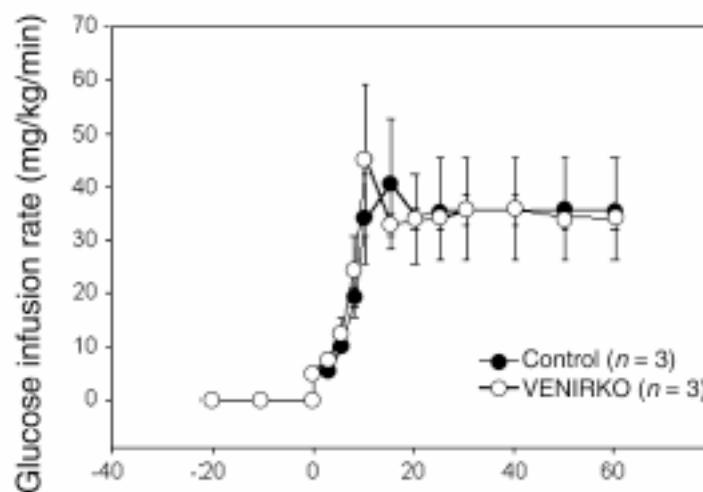
## Insulin Receptor

b



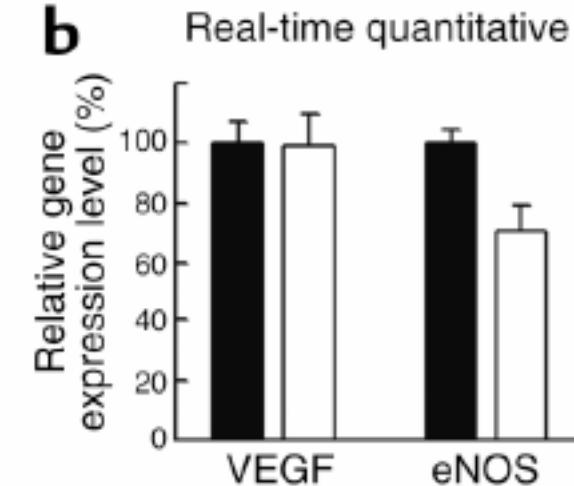
## Insulin Sensitivity

a



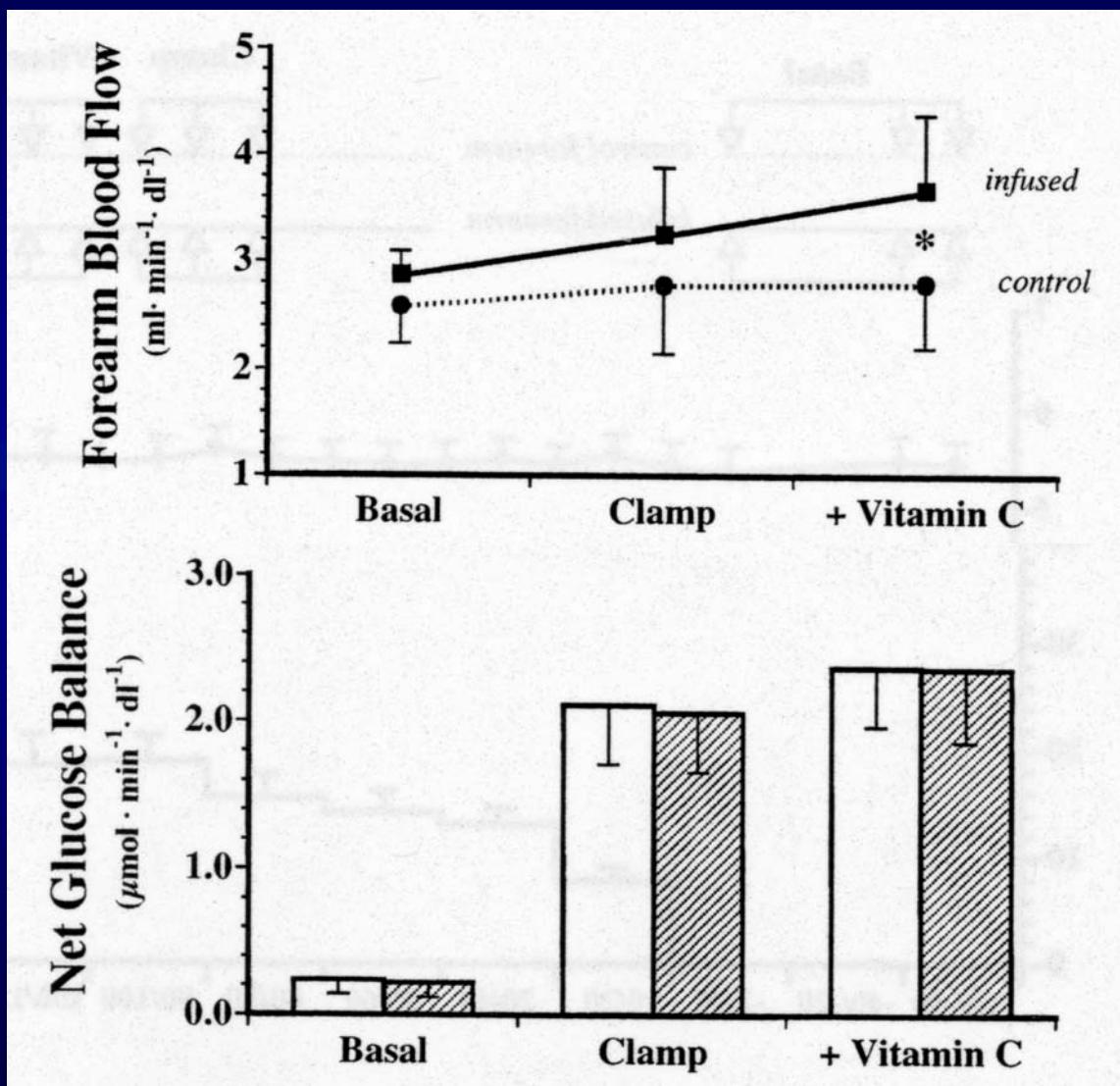
## NOS expression

b

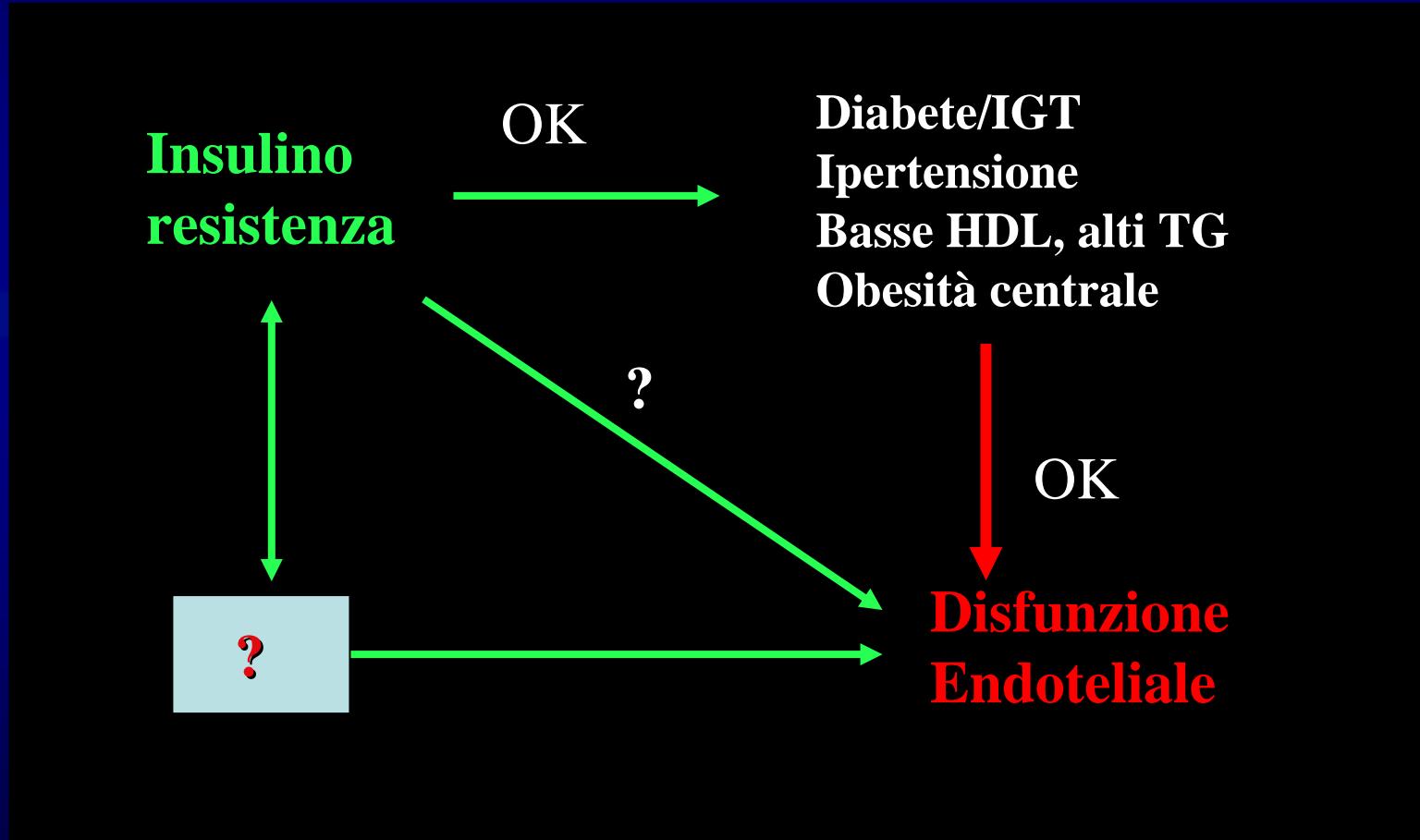


# Vit C restores EF but not IS in Ess. Hyp.

Natali A, ATVB 2000

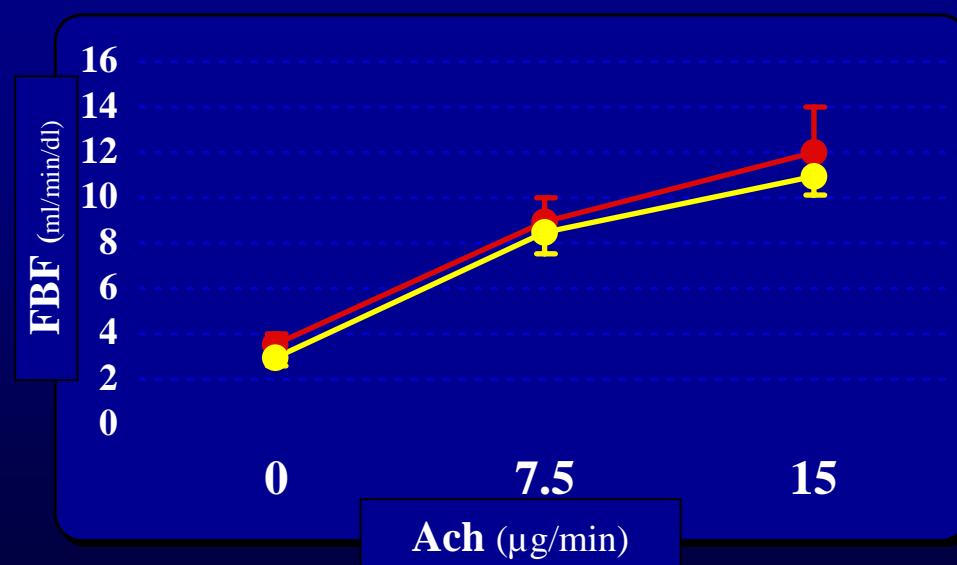
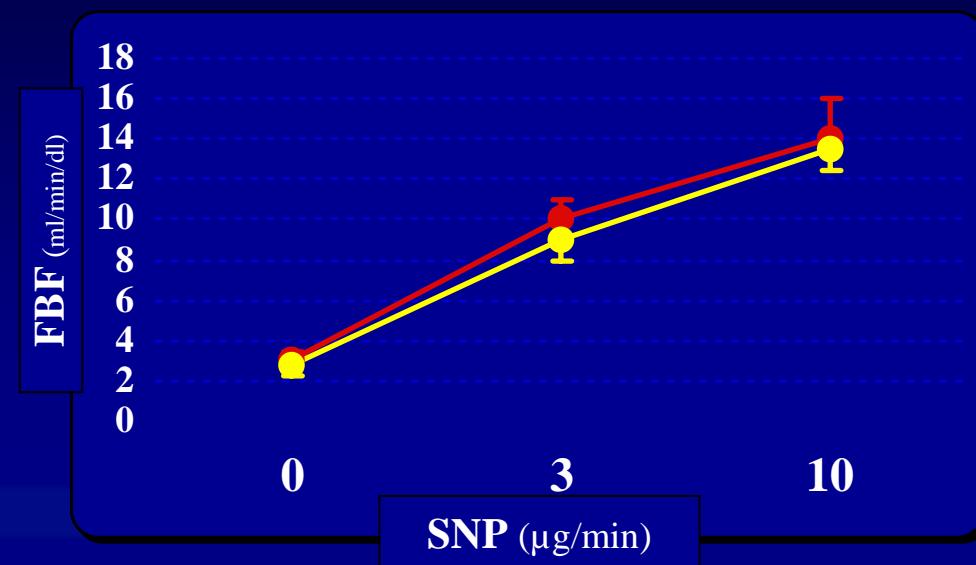
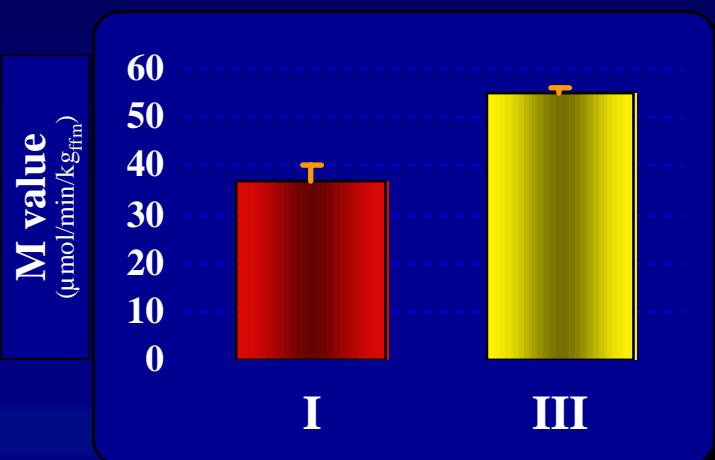


# Hipotesis: IR → ED



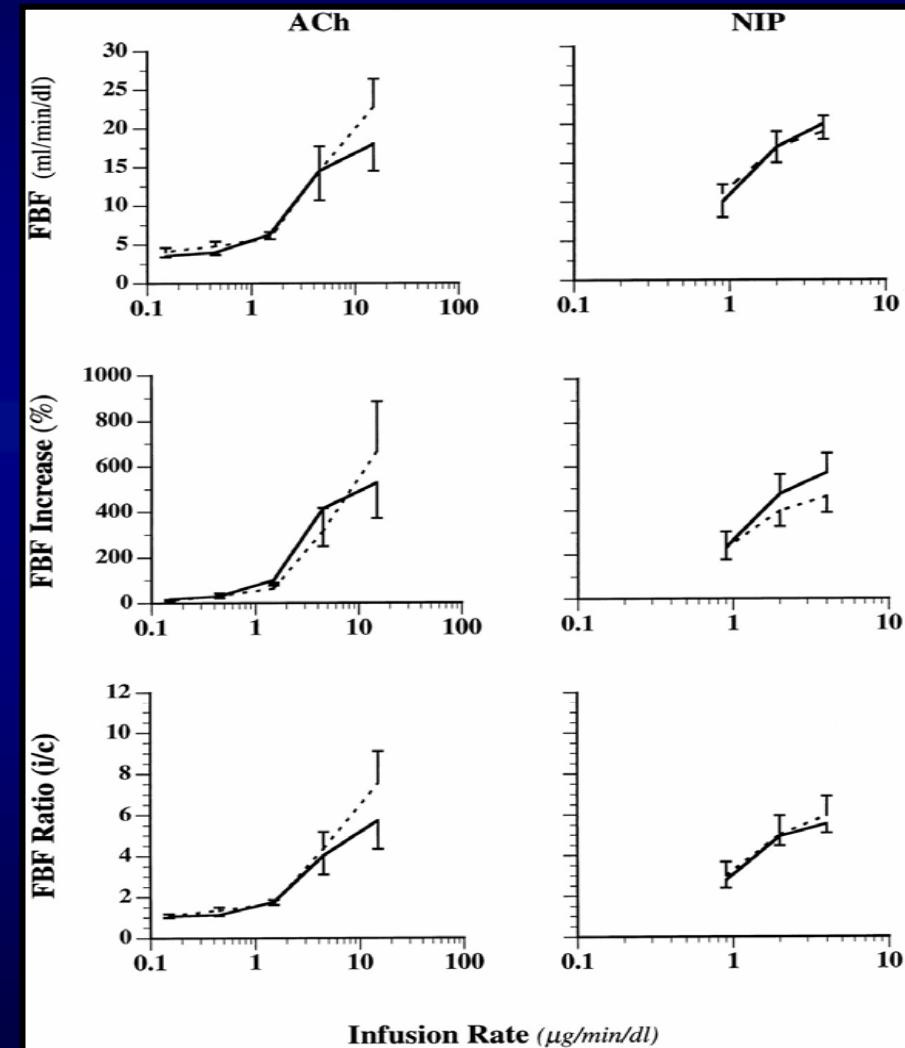
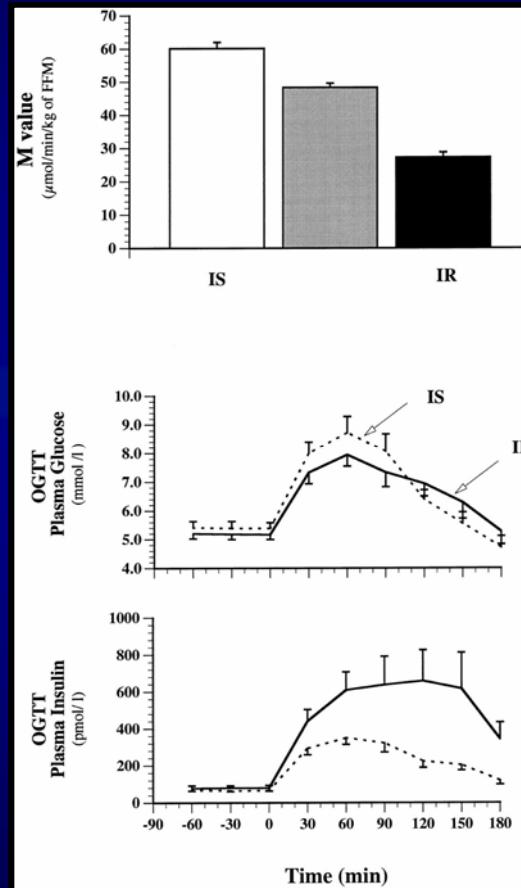
# Dissociation Between IR and ED in Normal Subjects

Forearm



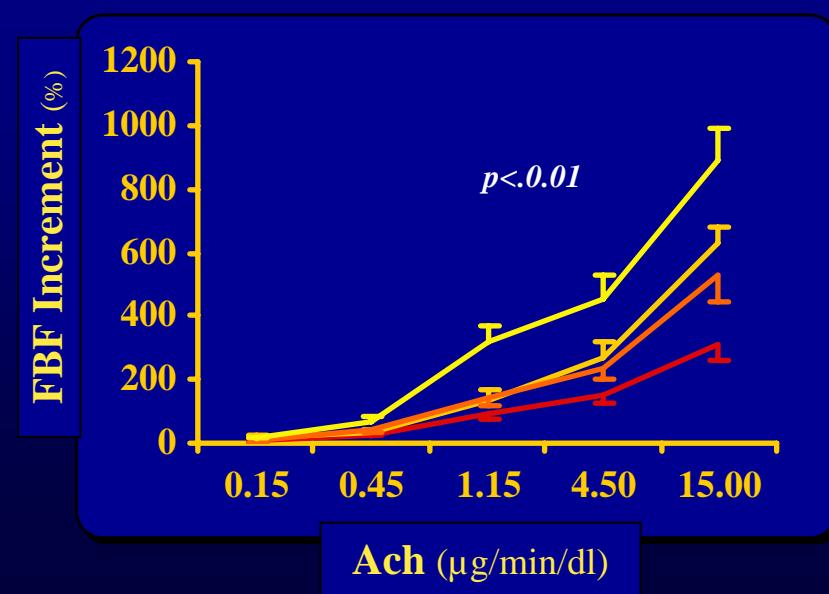
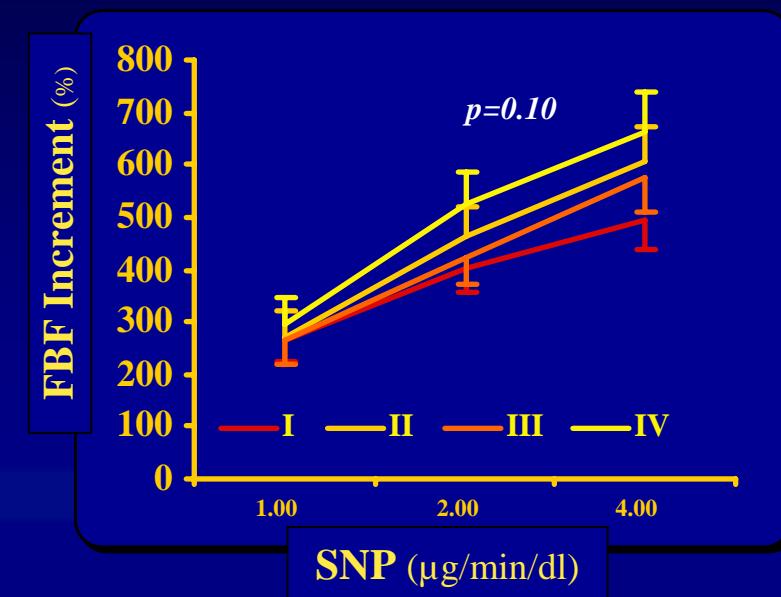
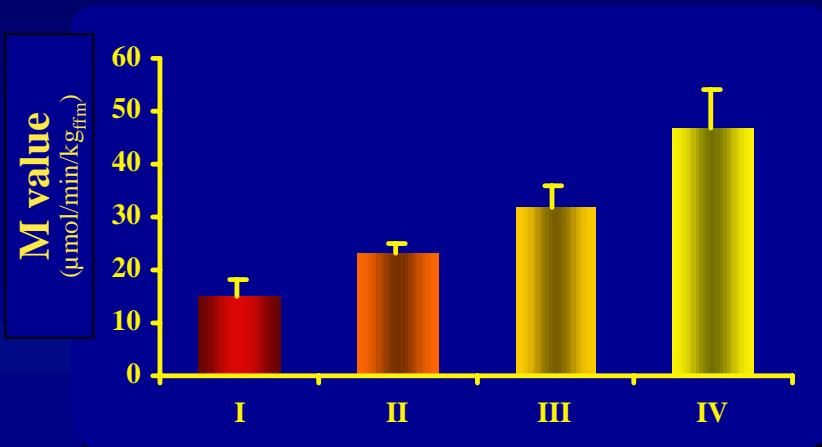
# Dissociation between IR and ED in Essential Hypertension

Forearm



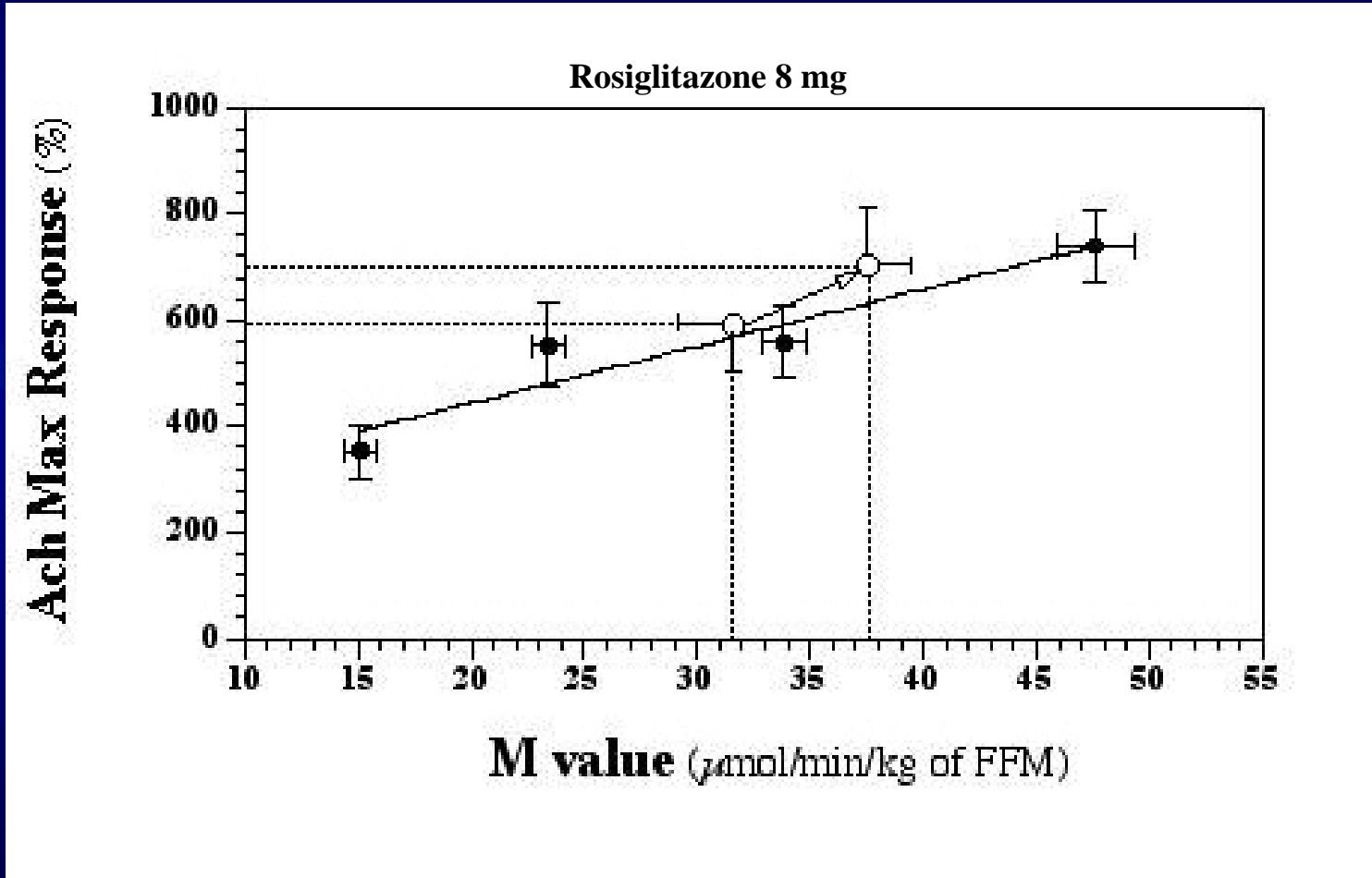
# *IR cosegregates with ED in NIDDM*

## Forearm



Natali A, (personal data)

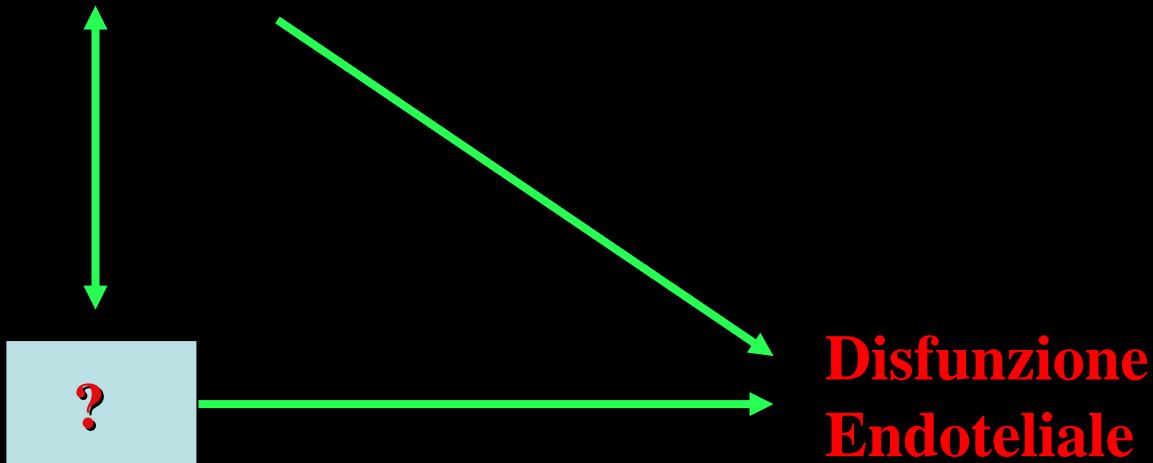
# *IR, ED and TZDs in NIDDM*



# Meccanismi

NIDDM

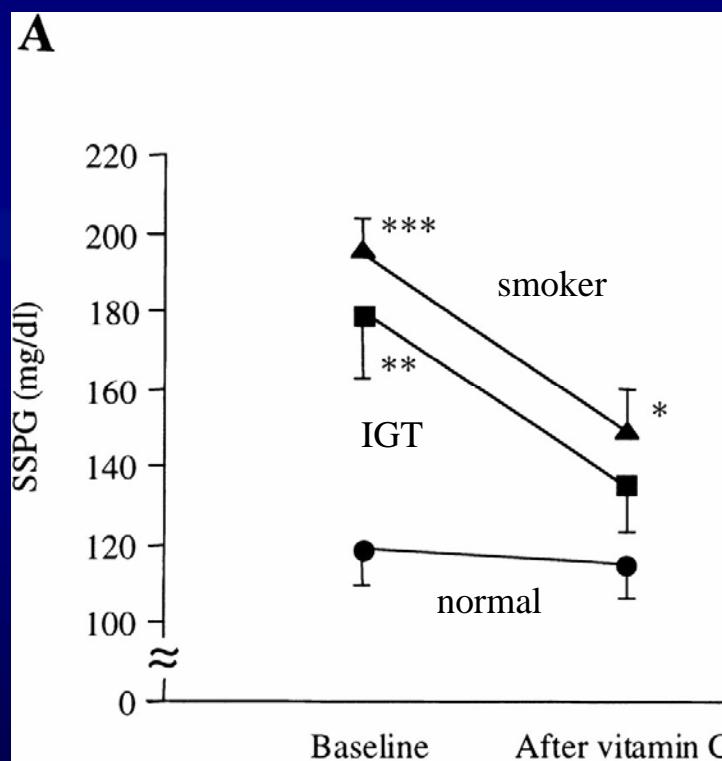
Insulino  
resistenza



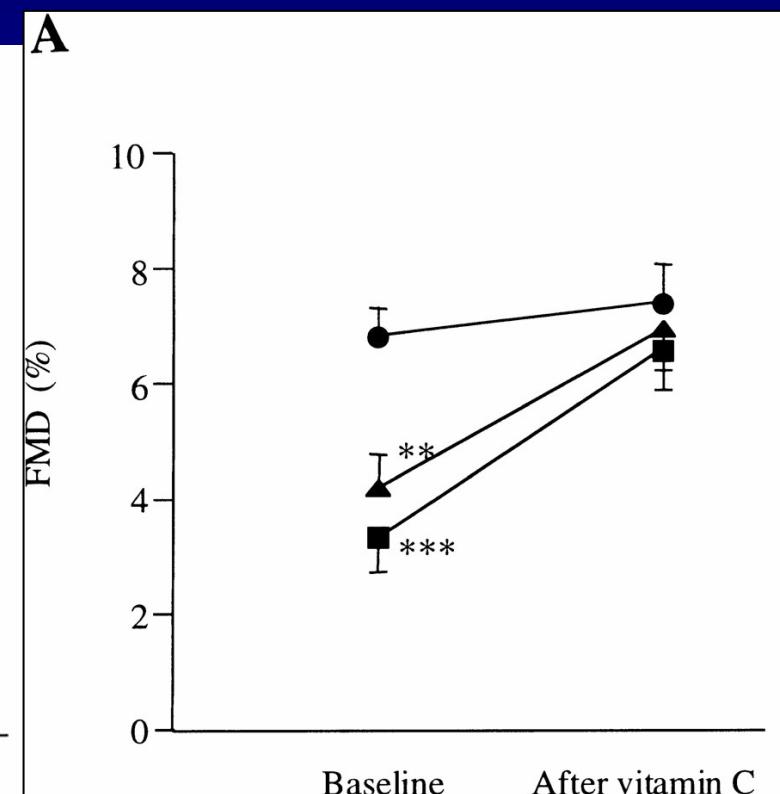
# Oxidative Stress

## Vitamin C (acute)

Reduces insulin resistance

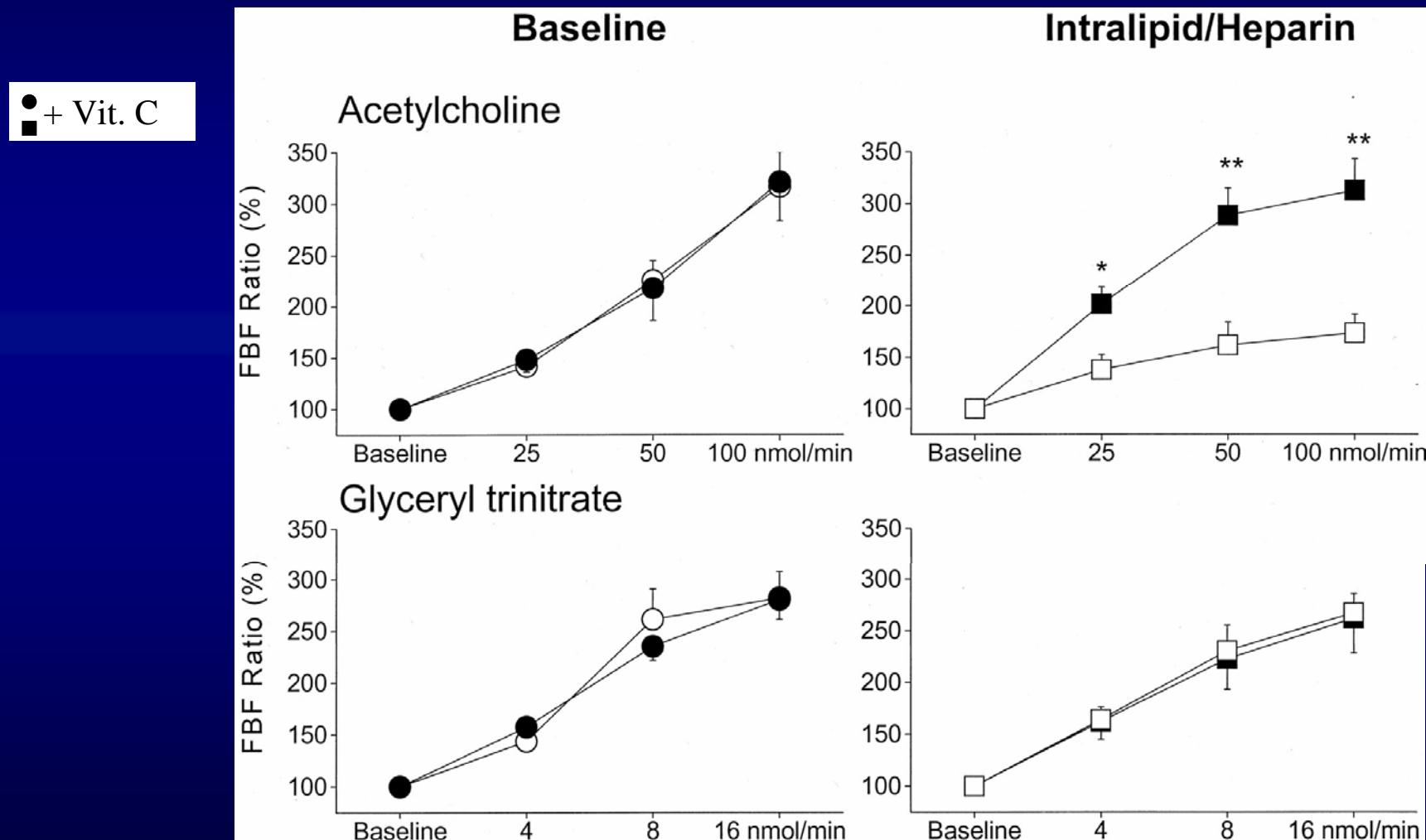


Improves Endothelial function

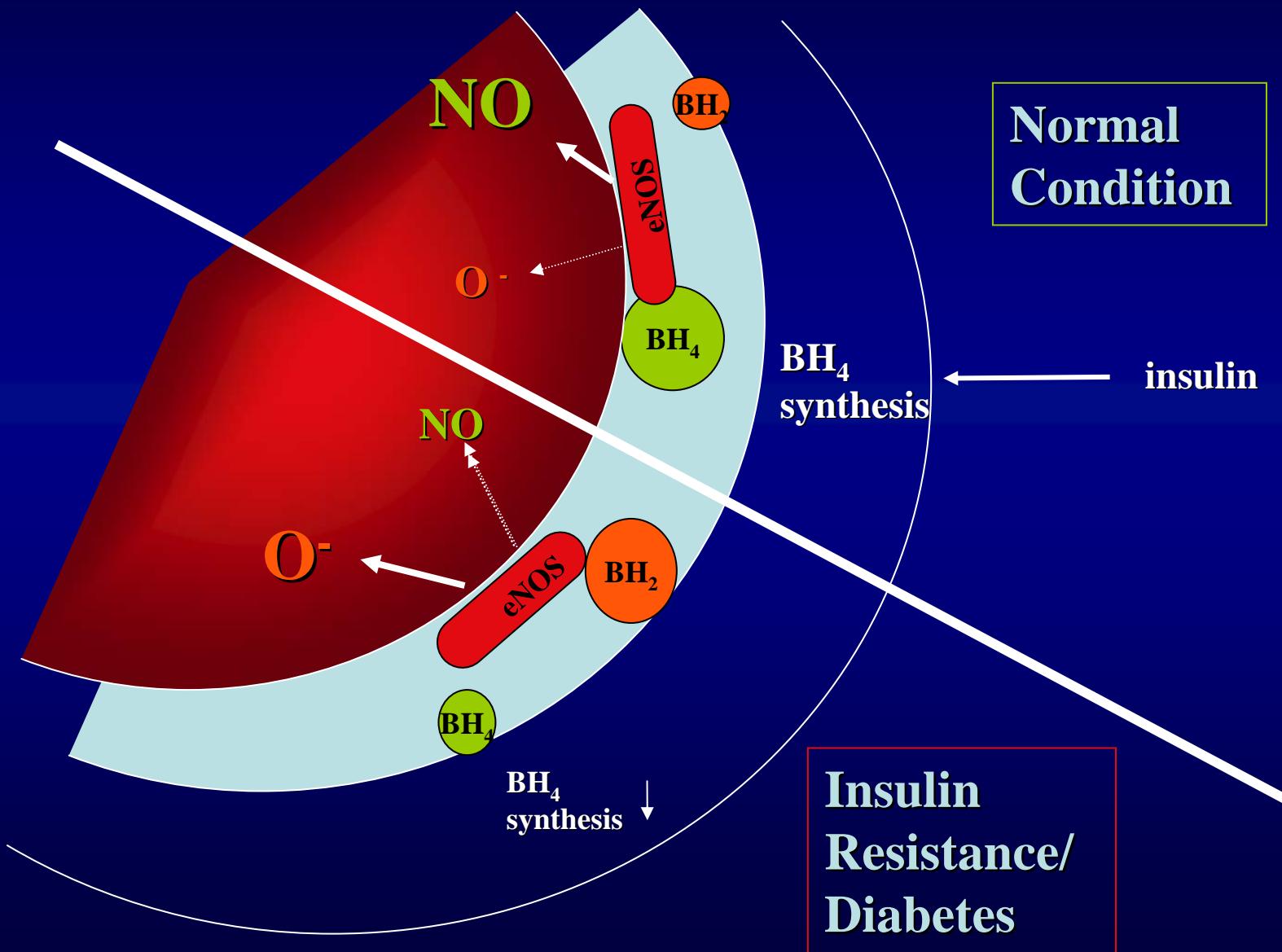


# FFA

FFA from  $320 \pm 64$  to  $1852 \pm 232$  uM

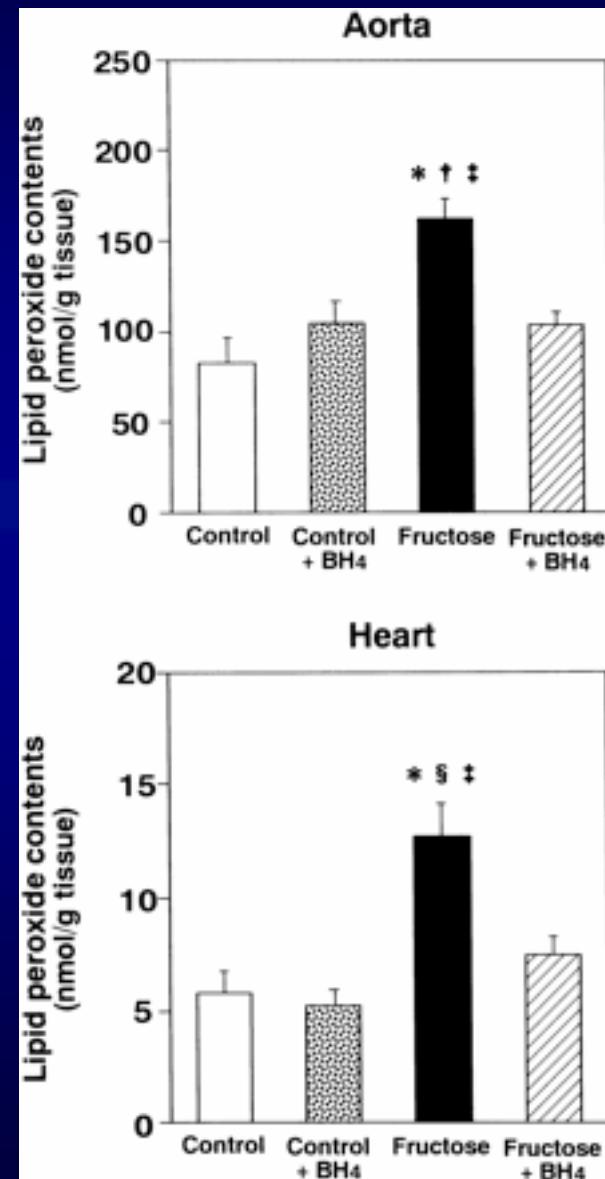
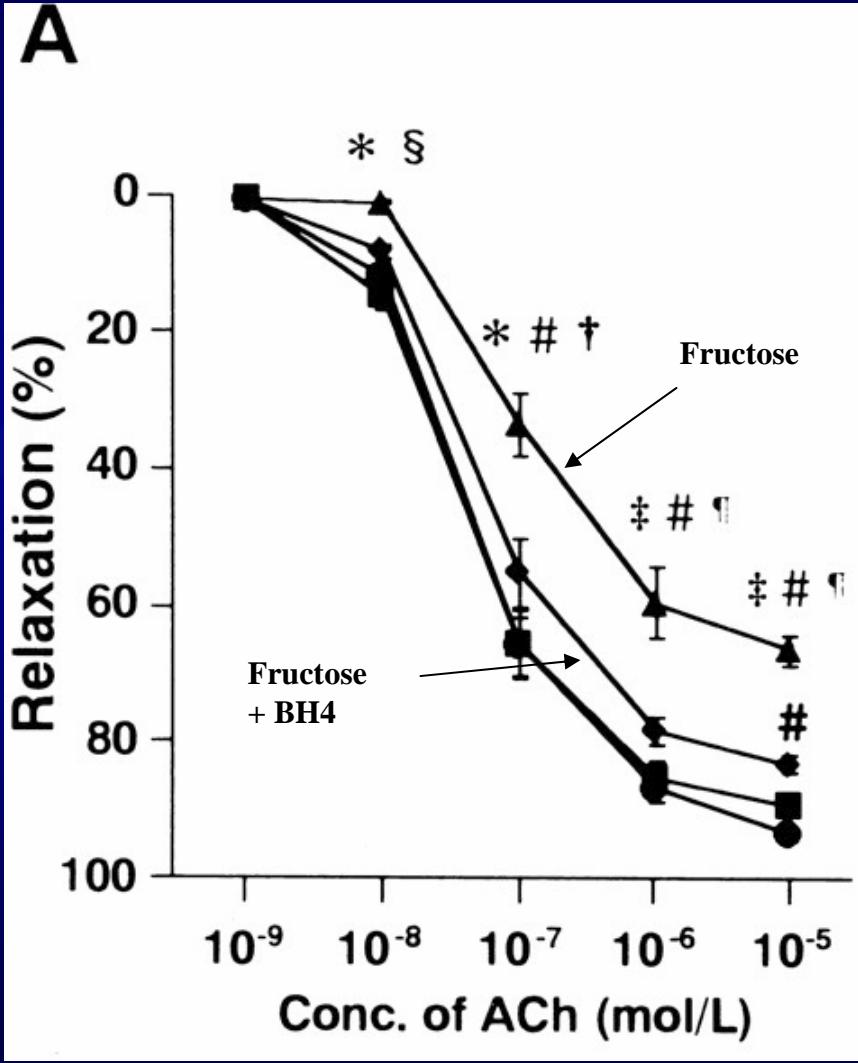


# Tetrahydrobiopterin ( $BH_4$ )



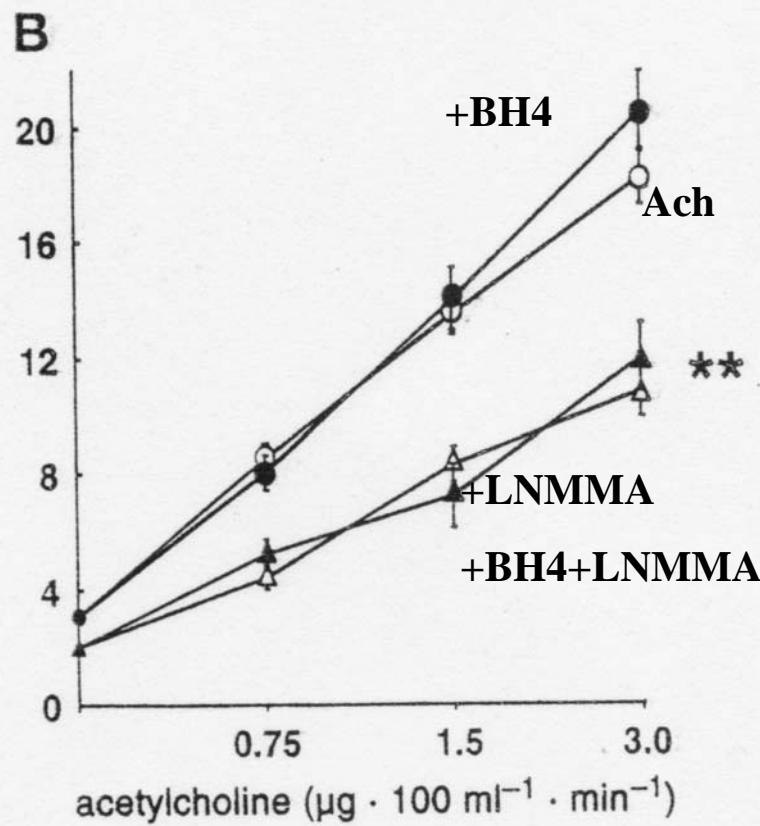
# *BH4 improves ED and Ox stress in IR diabetic animals*

aortic strips

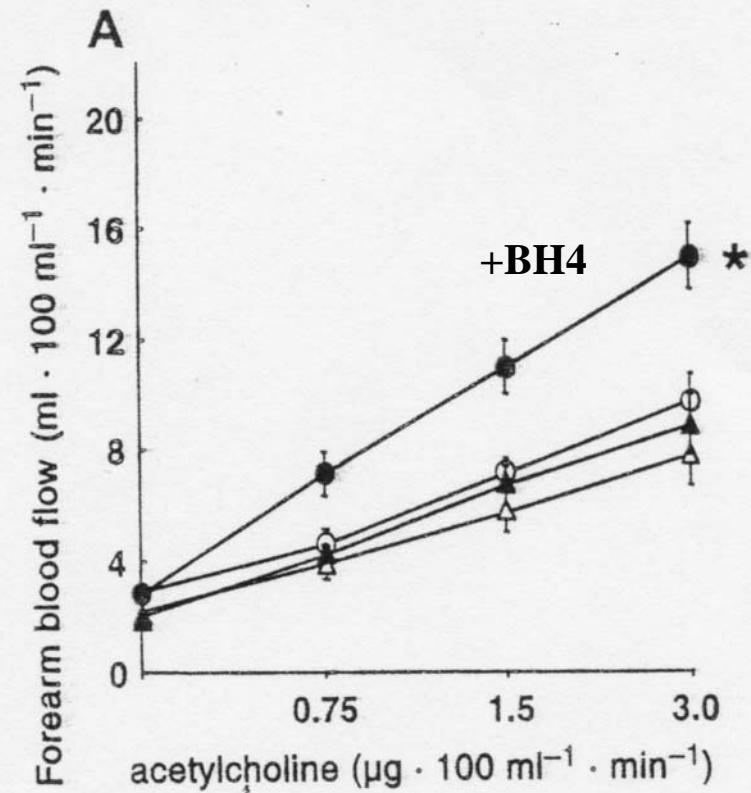


# BH4 improves ED in NIDDM

Control



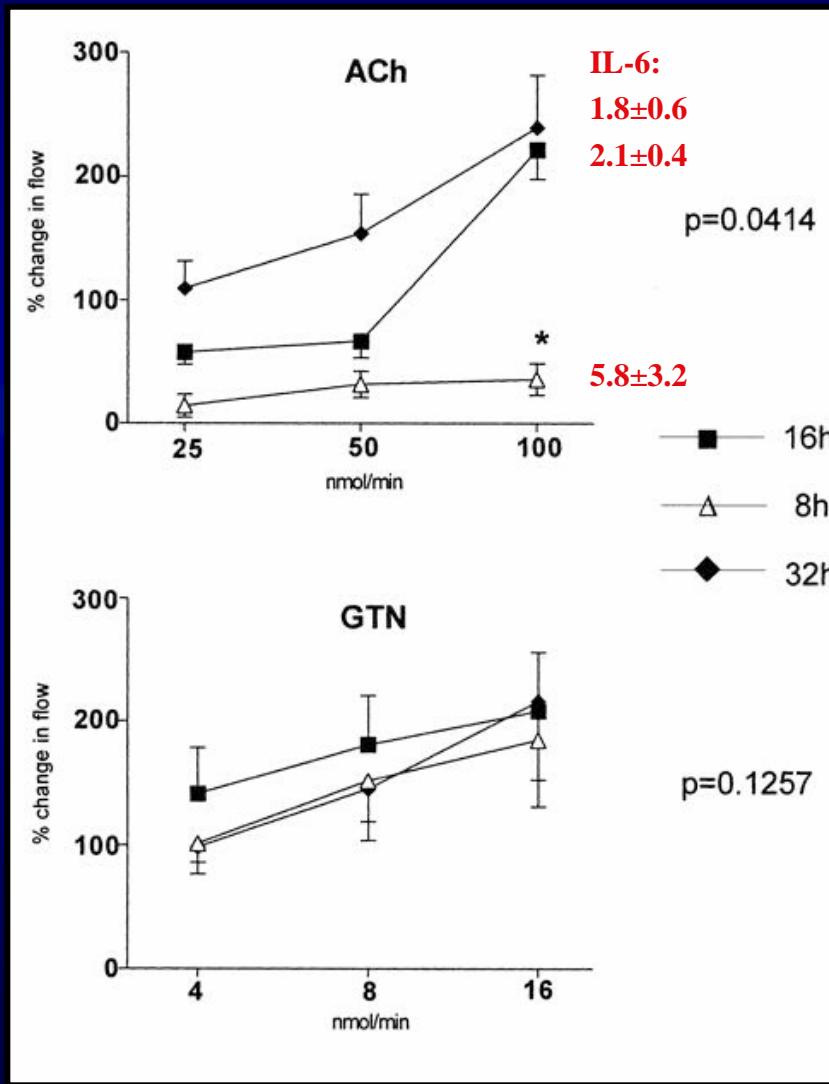
NIDDM



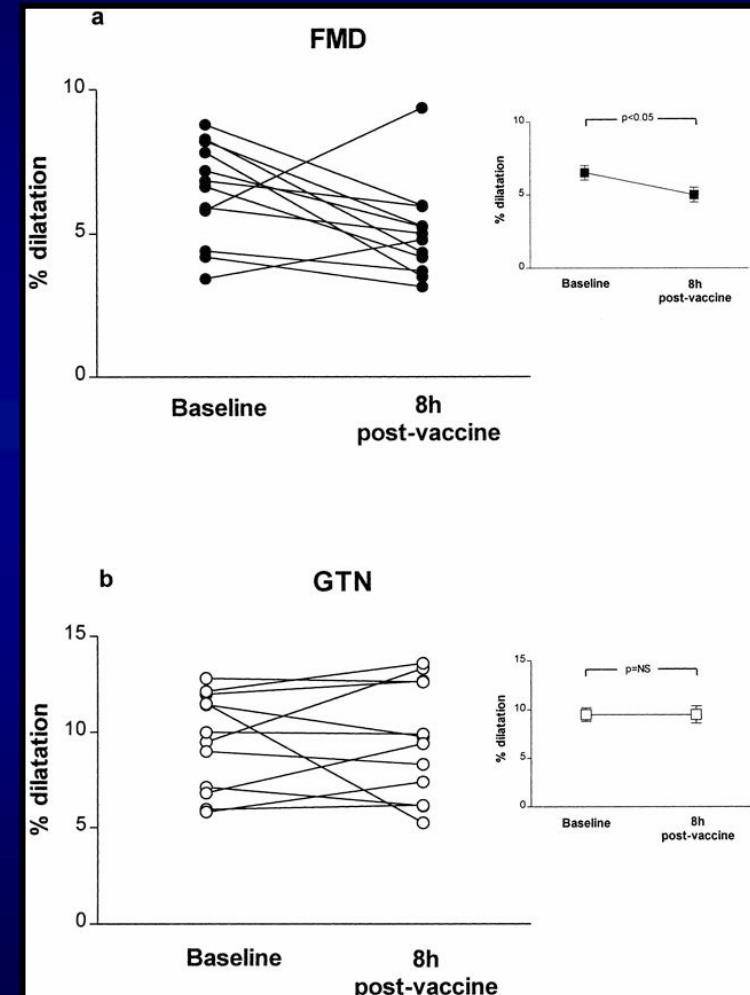
# Inflammation

FOREARM

Small vessels

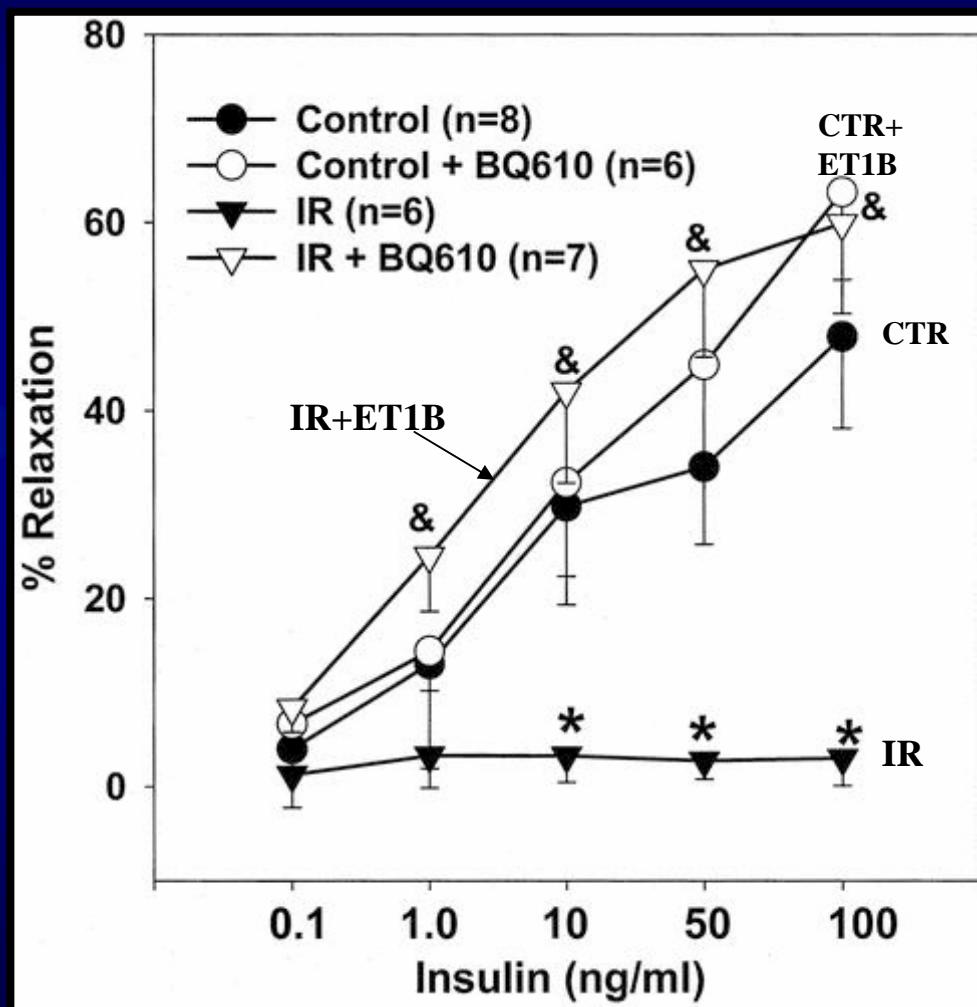


Large vessels

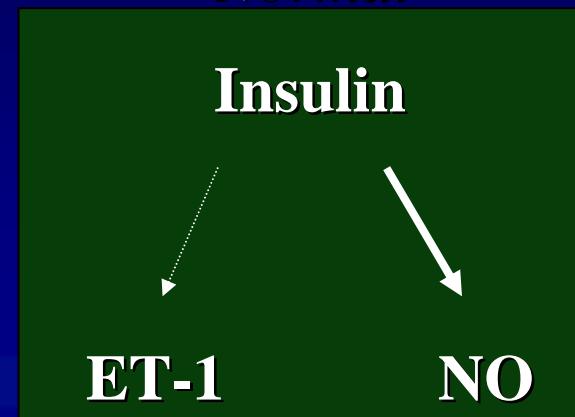


# Endothelin-1

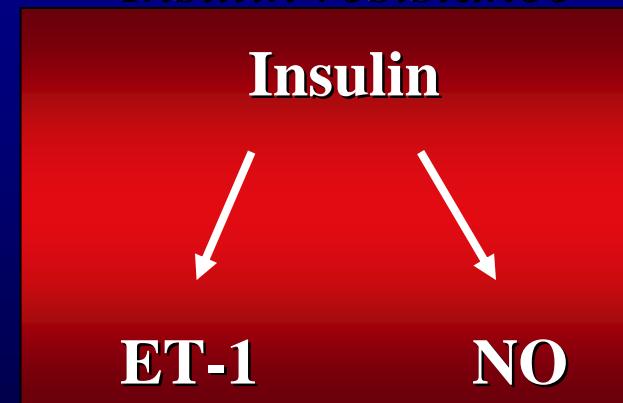
Mesenteric arteries



Normal

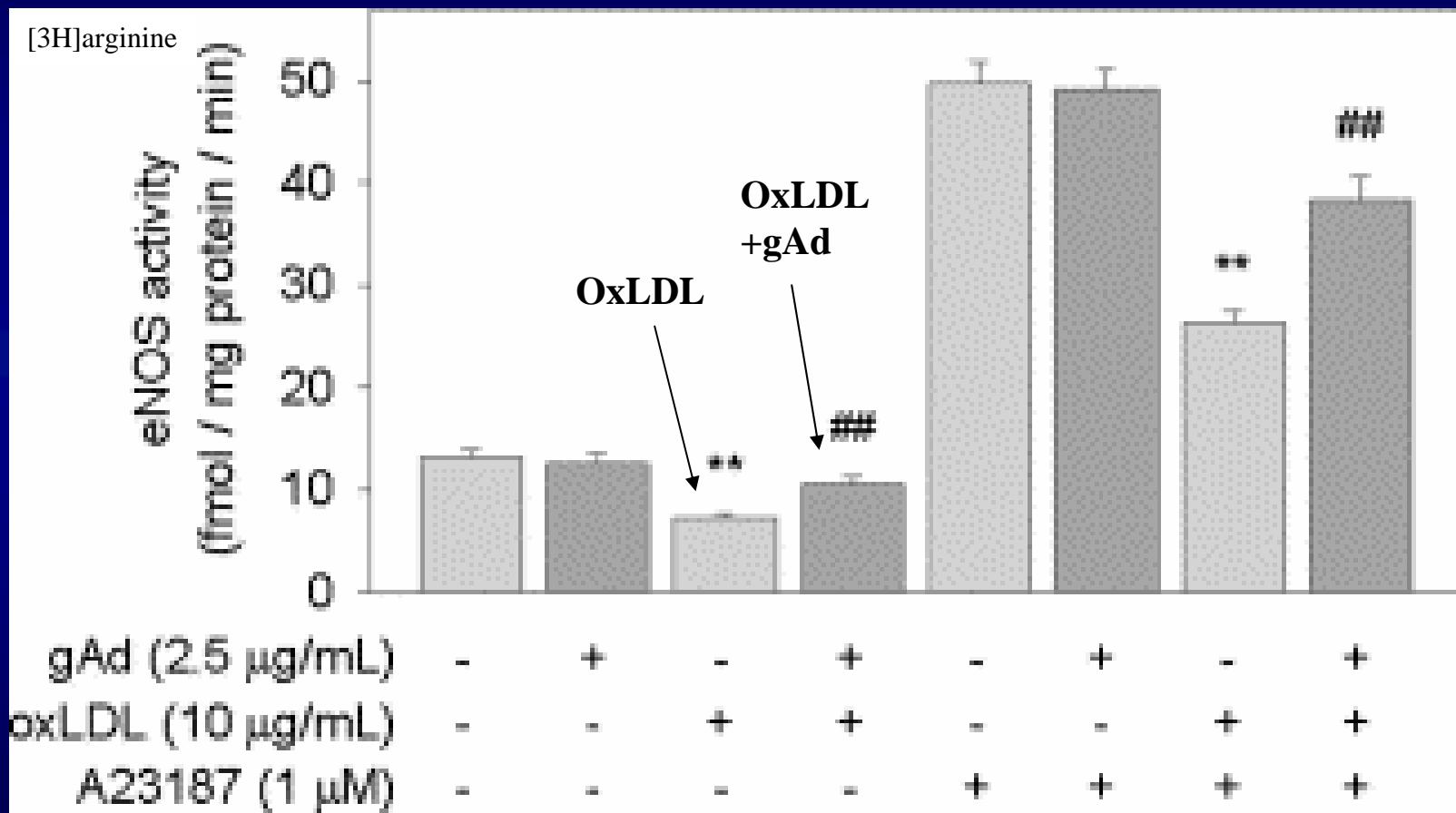


*Insulin resistance*



# Adiponectin

BAEC



# Conclusioni

