

The Rising Global Burden of Diabetes Mellitus

- > 100 million patients with DM
- 2.1% of worldwide population
- 90-95 % are affected by type 2
- ~ 221 millions estimated by 2010

Amos et al. Diab Med 1997

The Morbid Constellation

- **Obesity**
- **Hypertension**
- **Glucose Intolerance**
- **Insulin Resistance**
- **Dyslipidemia:**
 - (TG-rich lipoproteins
 - low levels of atheroprotective HDL
 - small, dense LDL particles)

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ROLE OF ENDOTHELIUM-DERIVED VASOACTIVE SUBSTANCES FROM PHYSIOLOGY TO ATHEROSCLEROTIC VASCULAR DISEASE

Relaxing factors

NO

PGI₂

EDHF

Growth inhibitors

NO

Contracting factors

Endothelin

TXA₂

PGH₂

O₂⁻

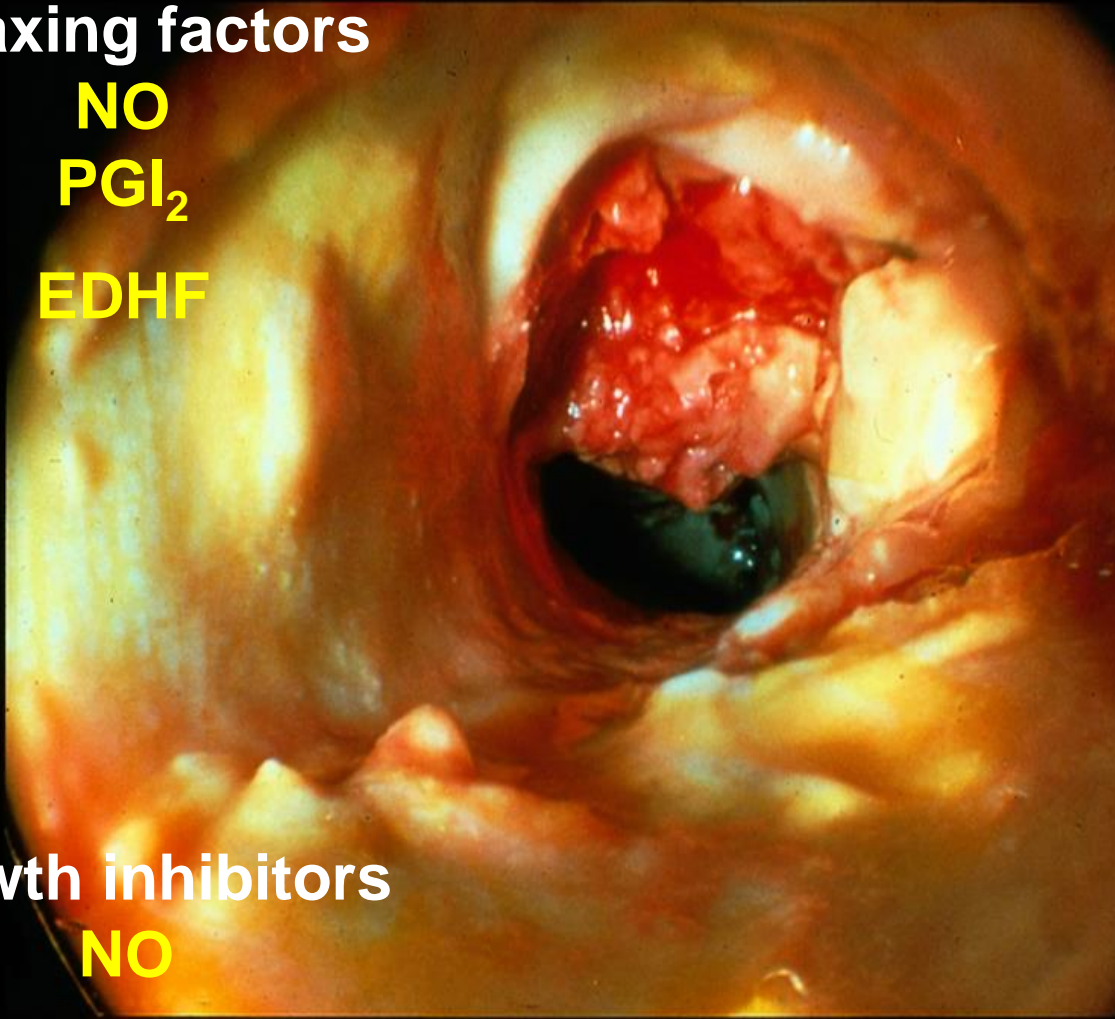
ATII

Growth promoters

Endothelin

O₂⁻

ATII



Baseline

Per vedere questa immagine
occorre QuickTime™ e un
decompressore Graphics.

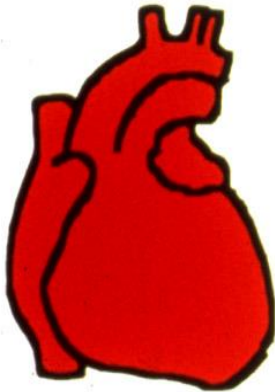
Acetylcholine

QuickTime™ and a
Graphics decompressor
are needed to see this picture.

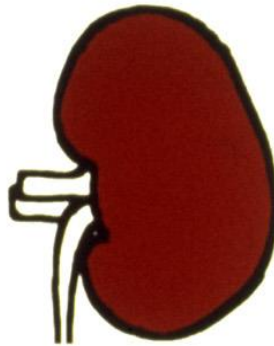
NTG i.c

QuickTime™ and a
Graphics decompressor
are needed to see this picture.

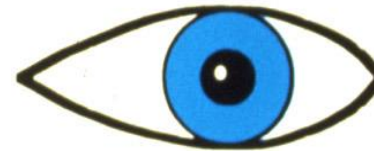
Diabetes



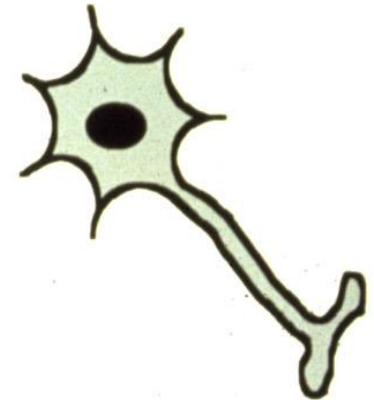
Endothelial
Dysfunction
Coronary Artery
Disease
Cardiac Failure



Proteinuria
Declining Kidney
Function
Renal Failure



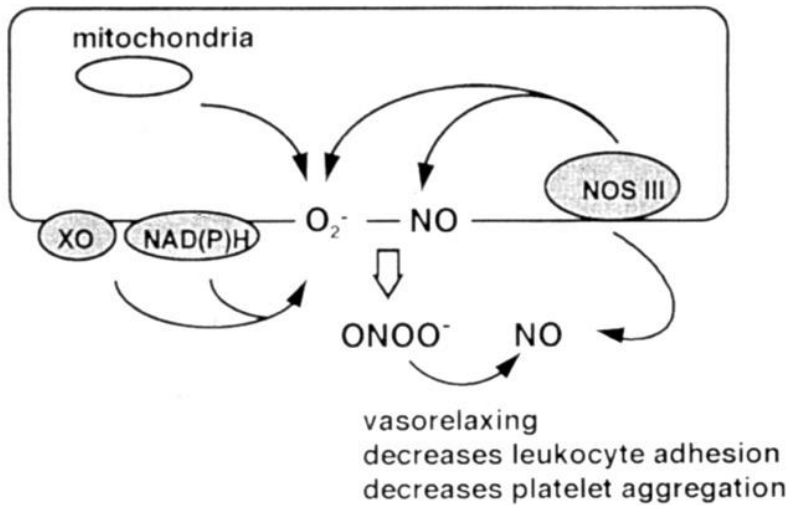
Retinopathy
Proliferative
Retinopathy
Blindness



Neuropathy

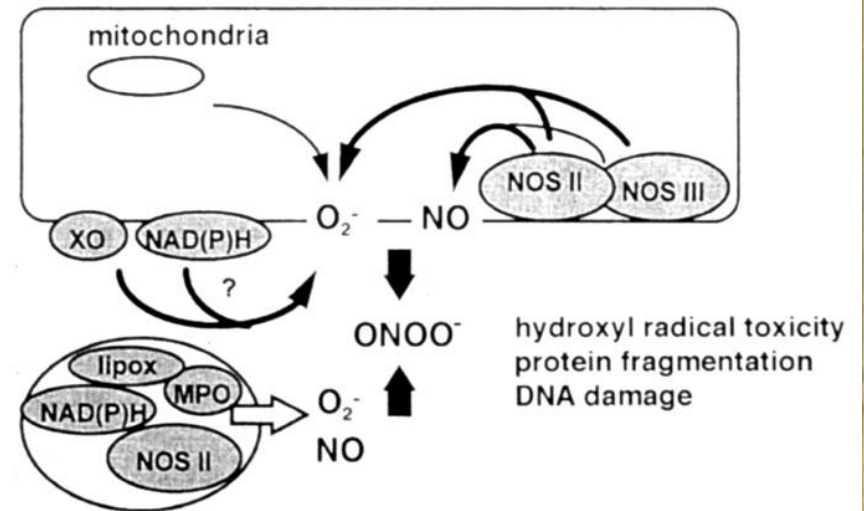
Physiology

Low Concentrations of Peroxynitrite

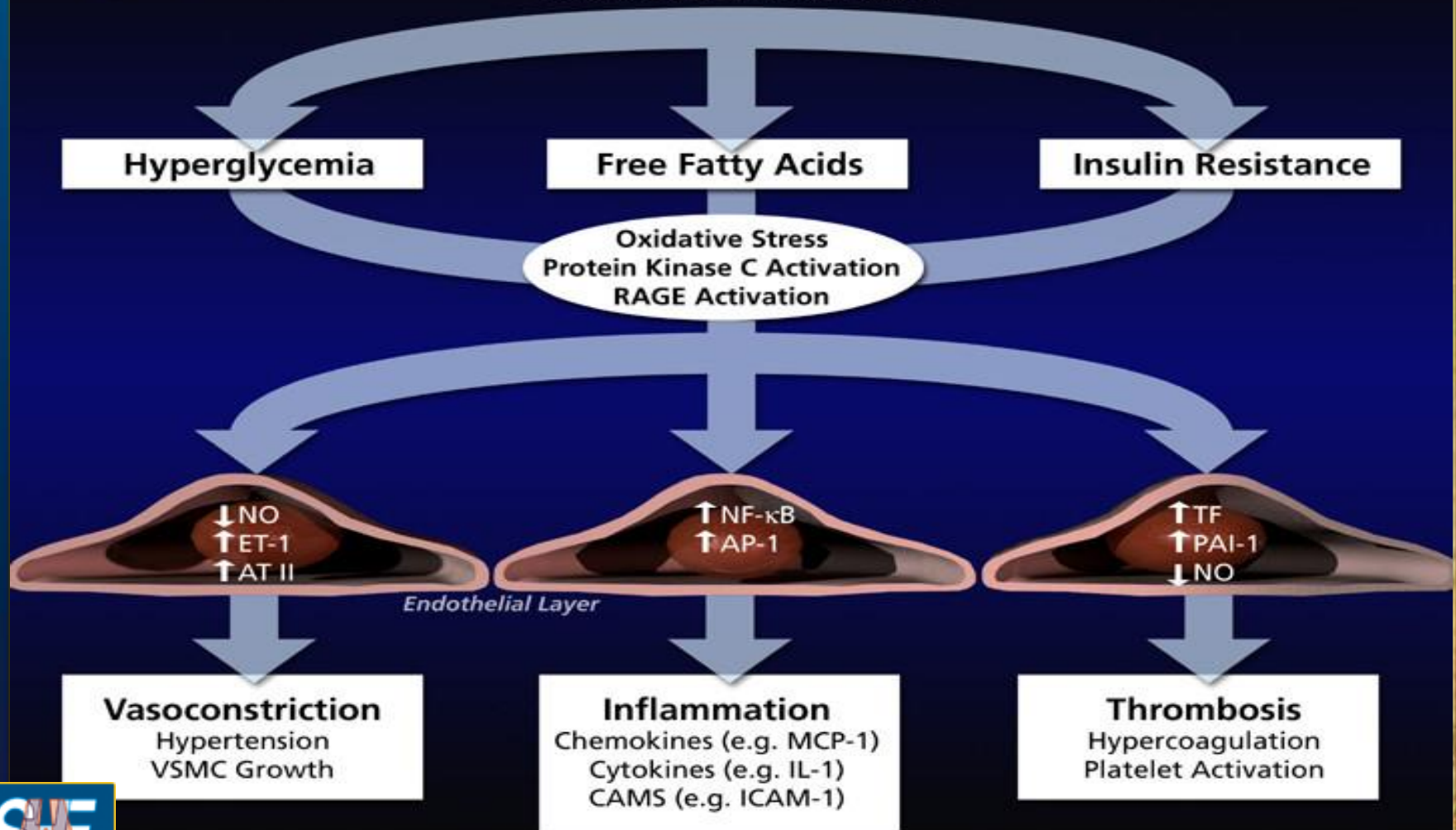


Atherosclerosis

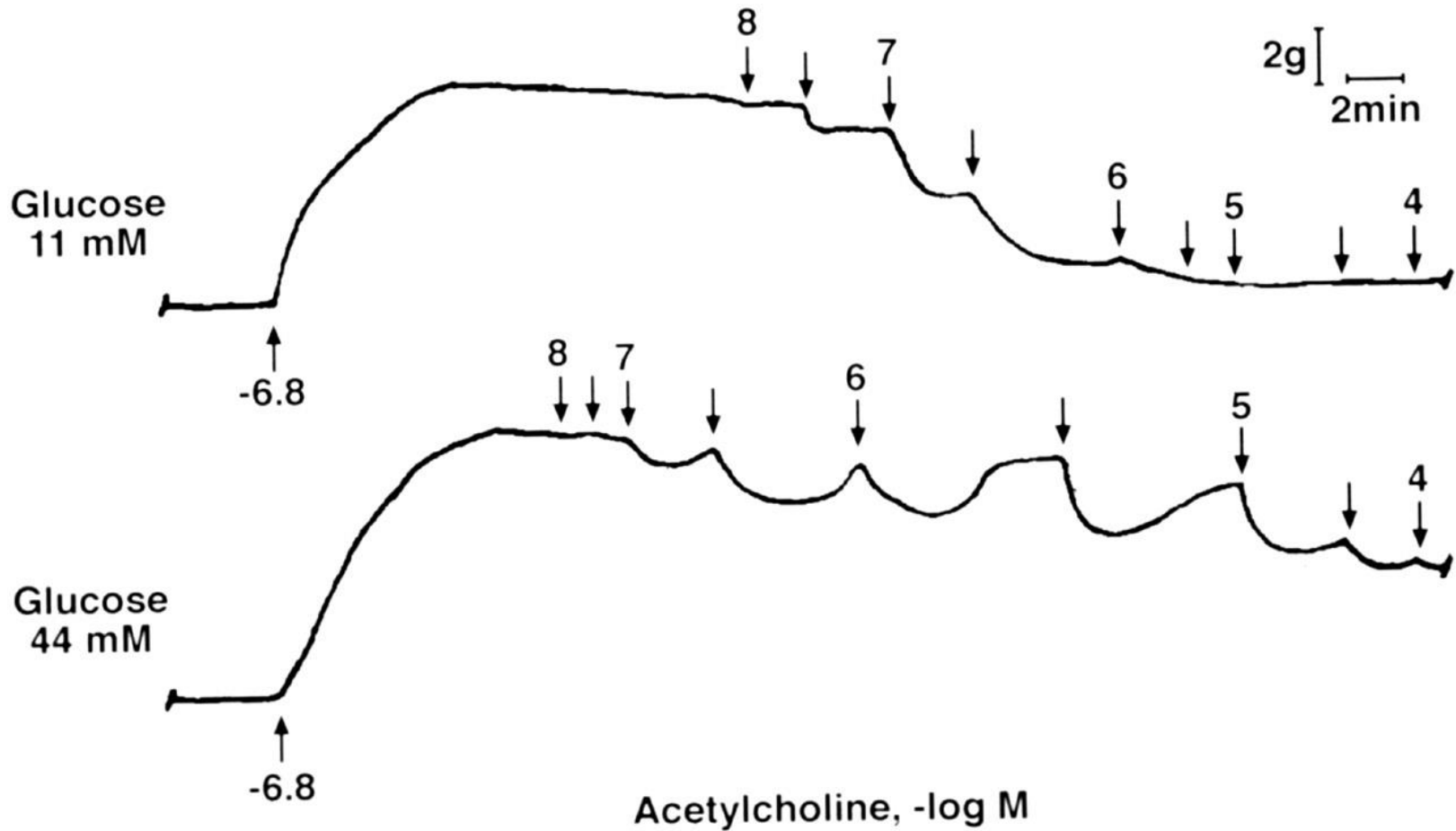
Formation of High Concentrations of Peroxynitrite



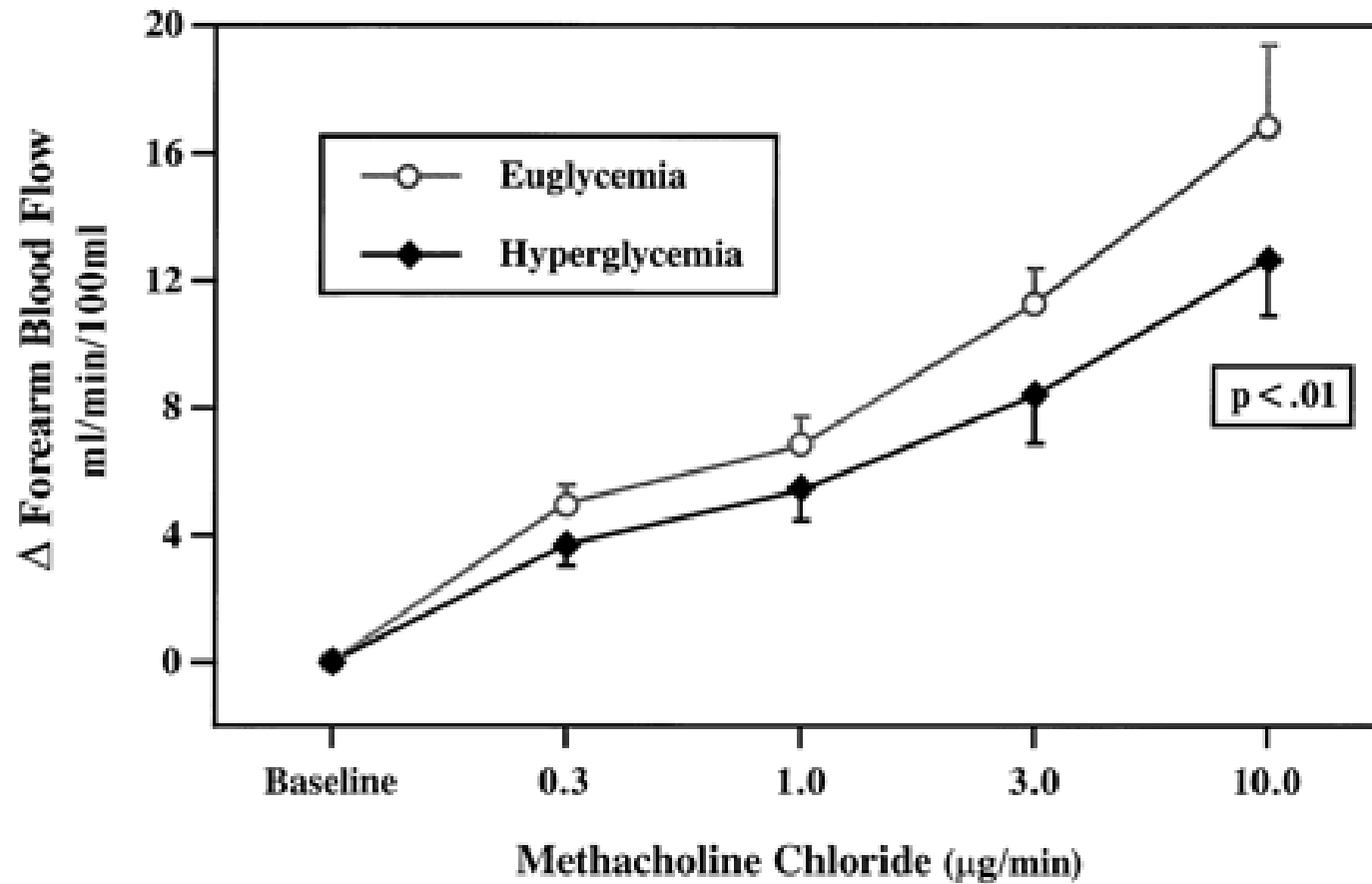
Diabetes Mellitus



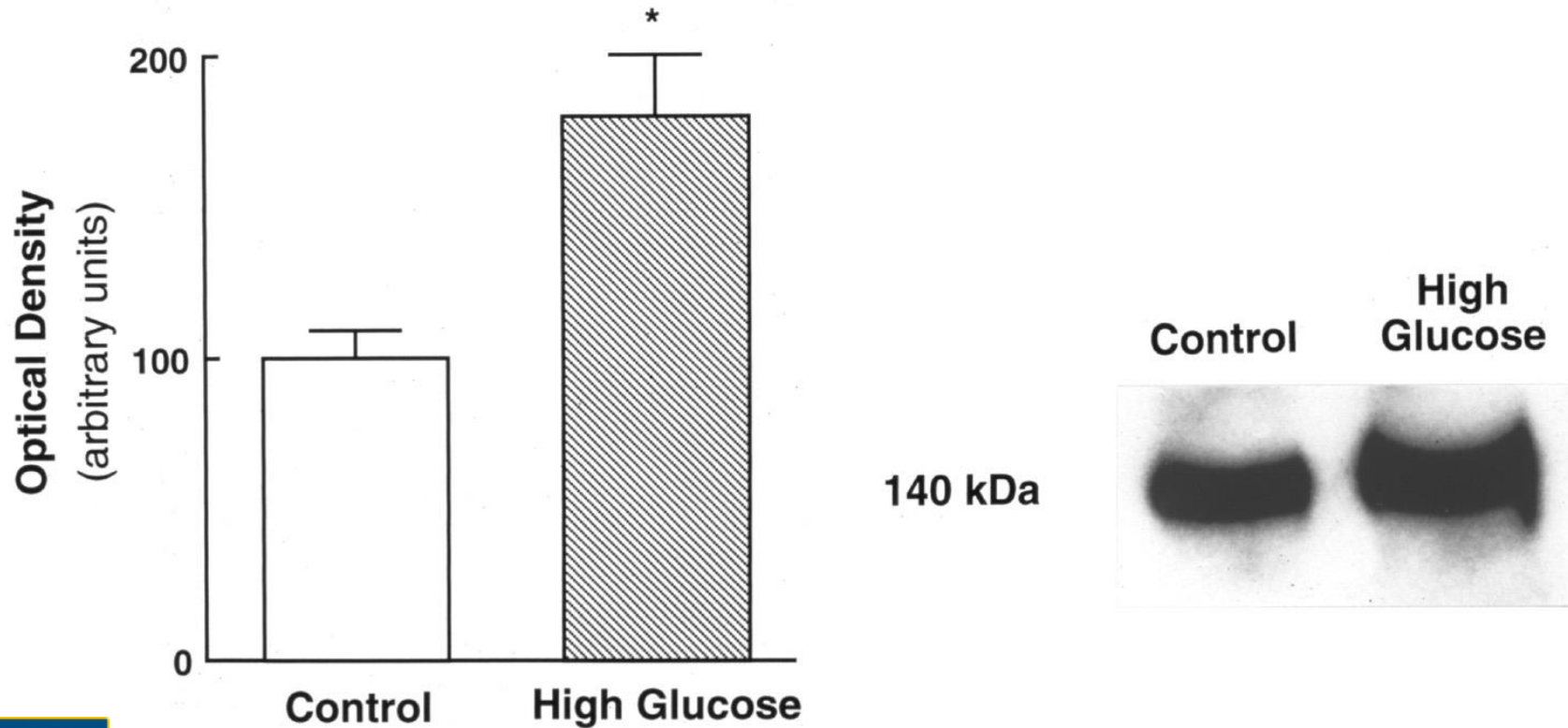
8 Exposure to Elevated Glucose and Endothelium-Dependent Relaxations to Acetylcholine in Rabbit Aorta



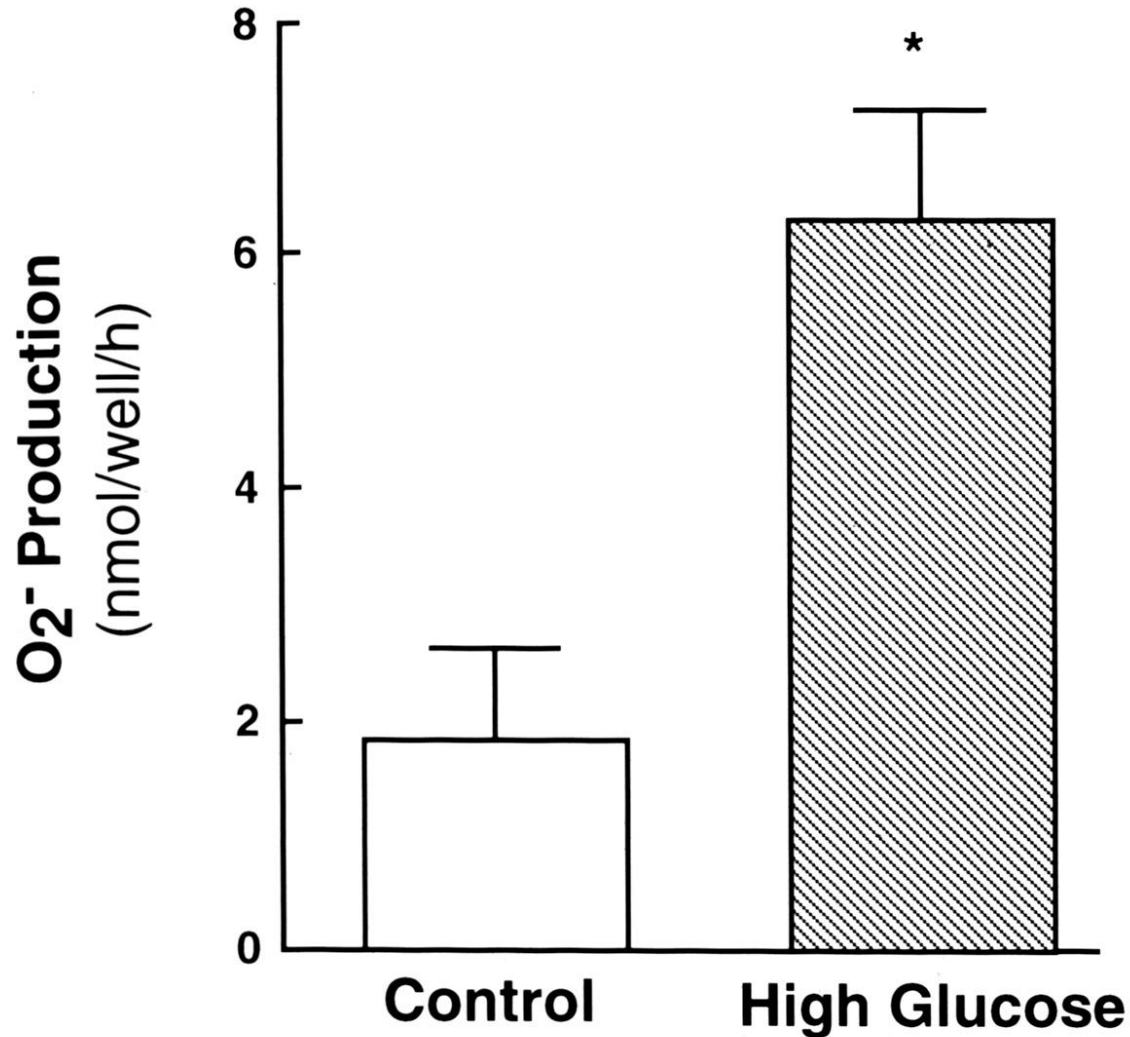
Hyperglycemia and Endothelium-Dependent Dilation



Effect of High Glucose on NO Synthase Expression in Human Aortic Endothelial Cells

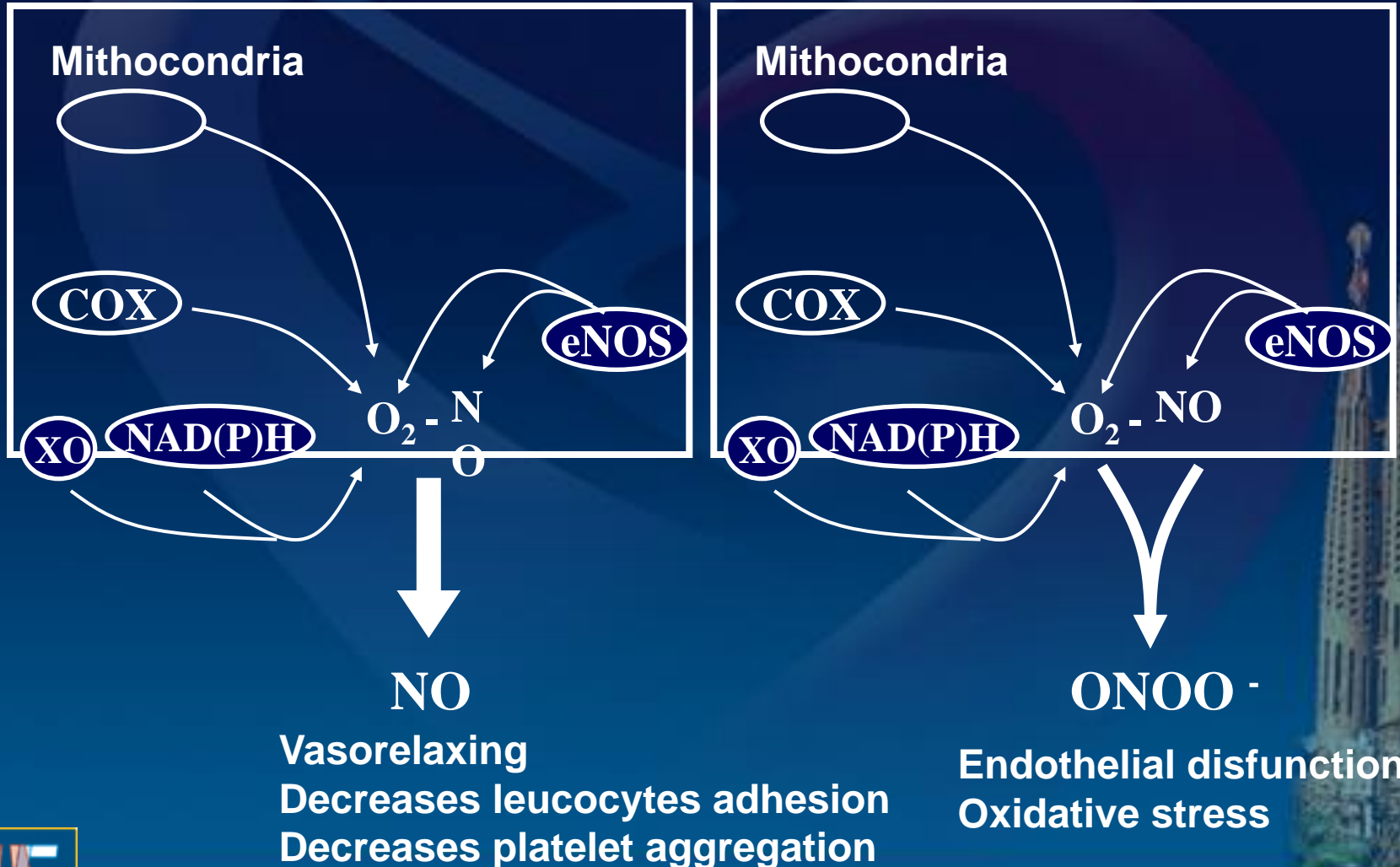


Effect of High Glucose on Superoxide Anion Production

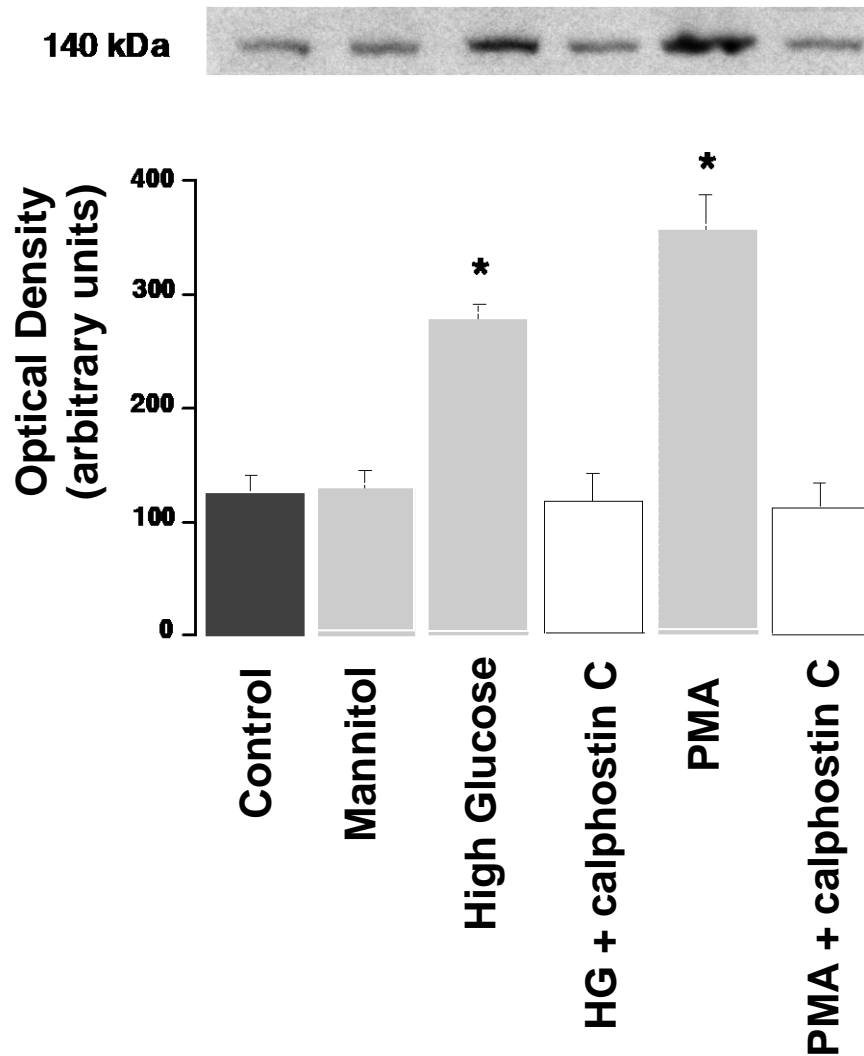


PHYSIOLOGY

HYPERGLYCEMIA

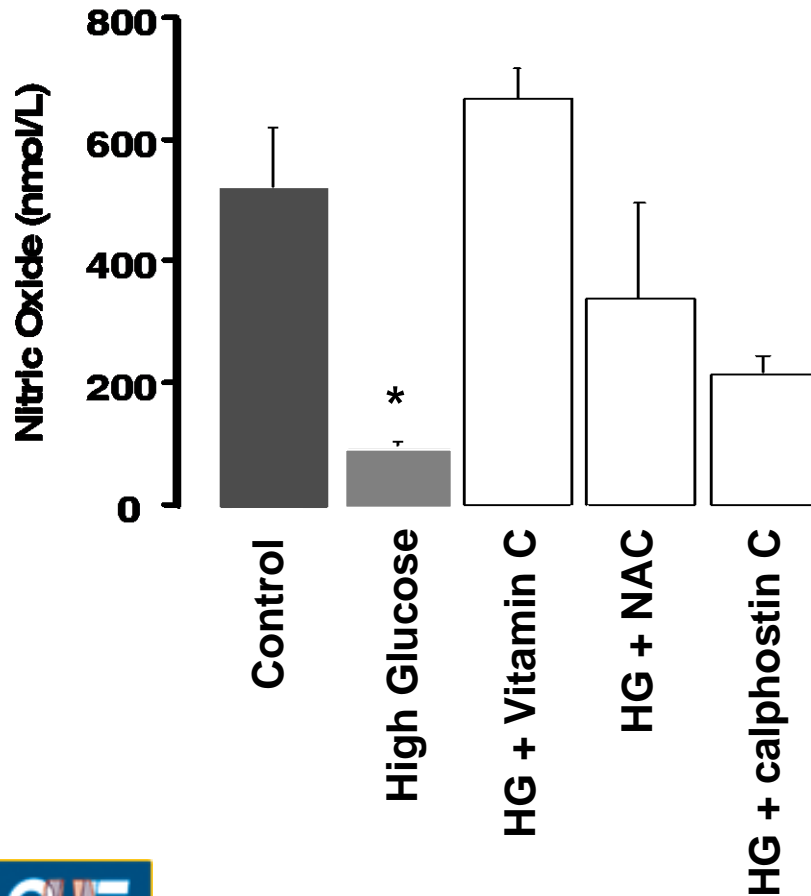


Protein Kinase C Regulates eNOS Expression in HAEC Exposed to High Glucose

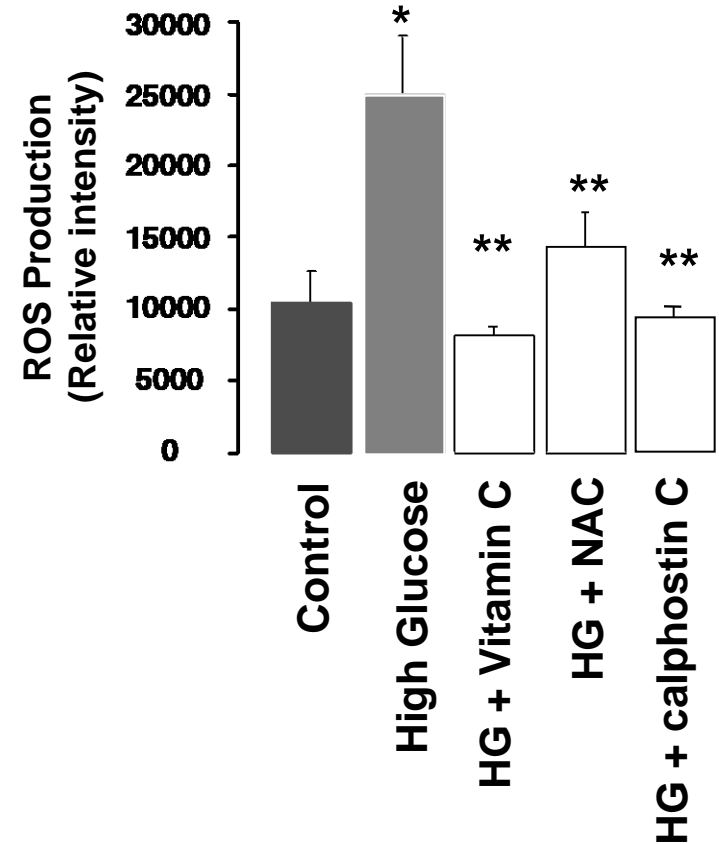


High Glucose and PKC-Dependent Effects

NO Concentrations

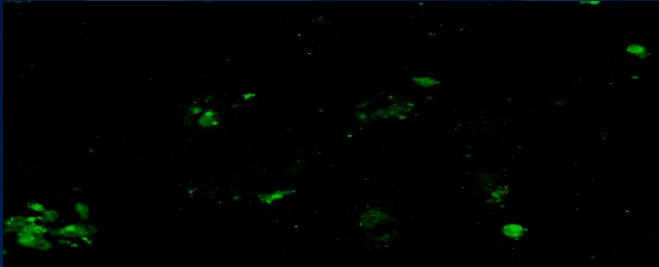


Reactive Oxygen Species



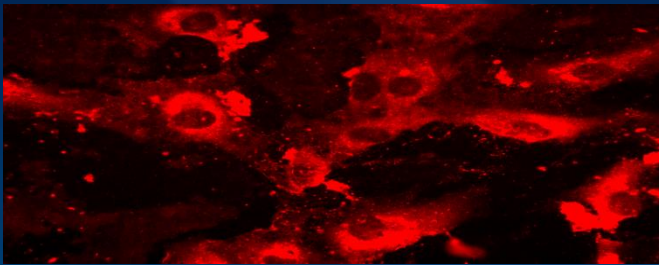
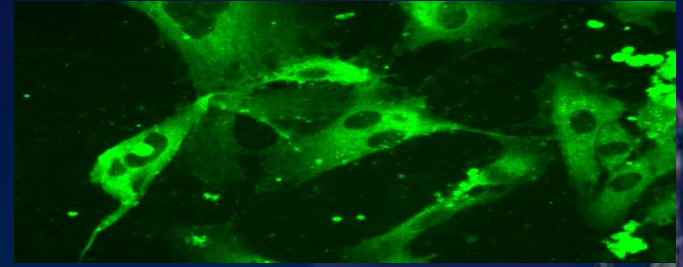
High Glucose Induces Tyrosine Nitration of PGI₂ synthase

Control

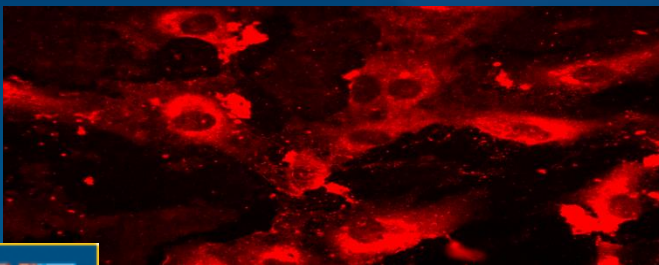
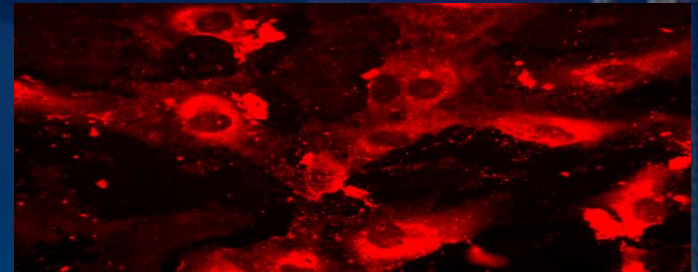


3-nitrotyrosine

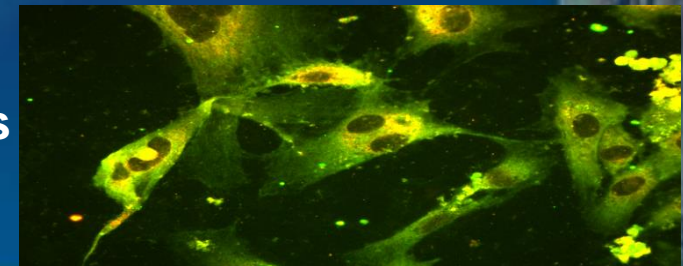
High Glucose



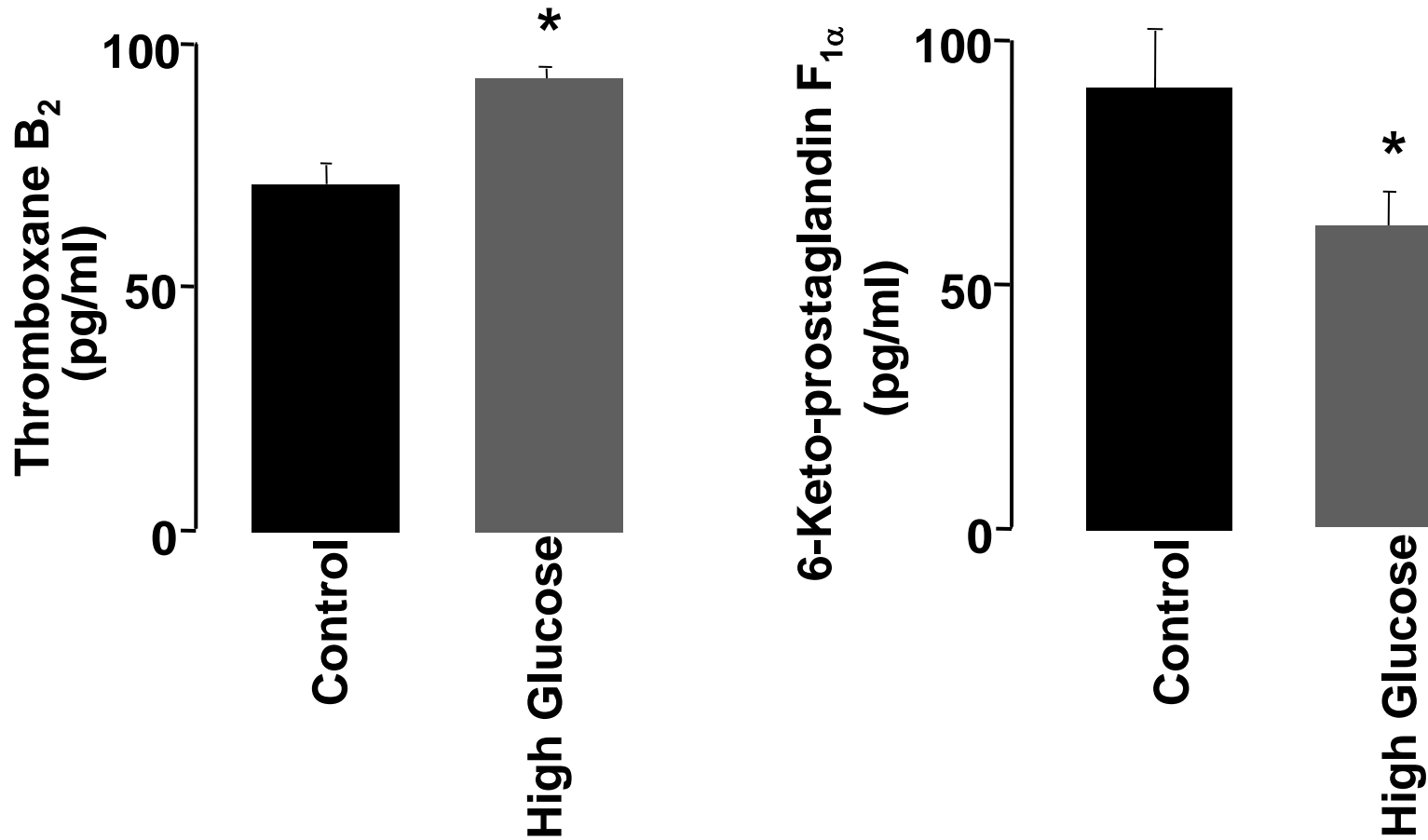
PGI₂ synthase



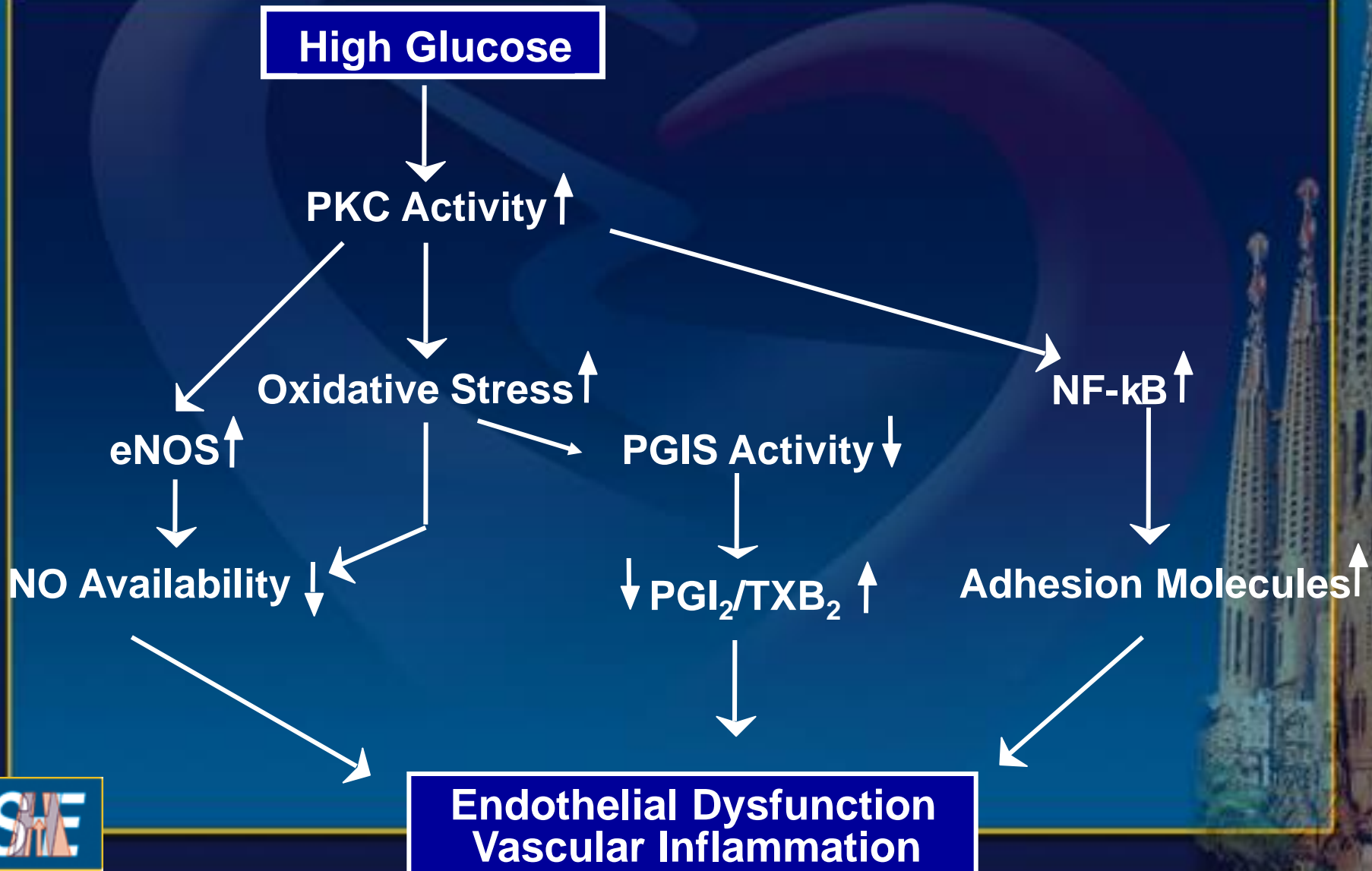
merged images



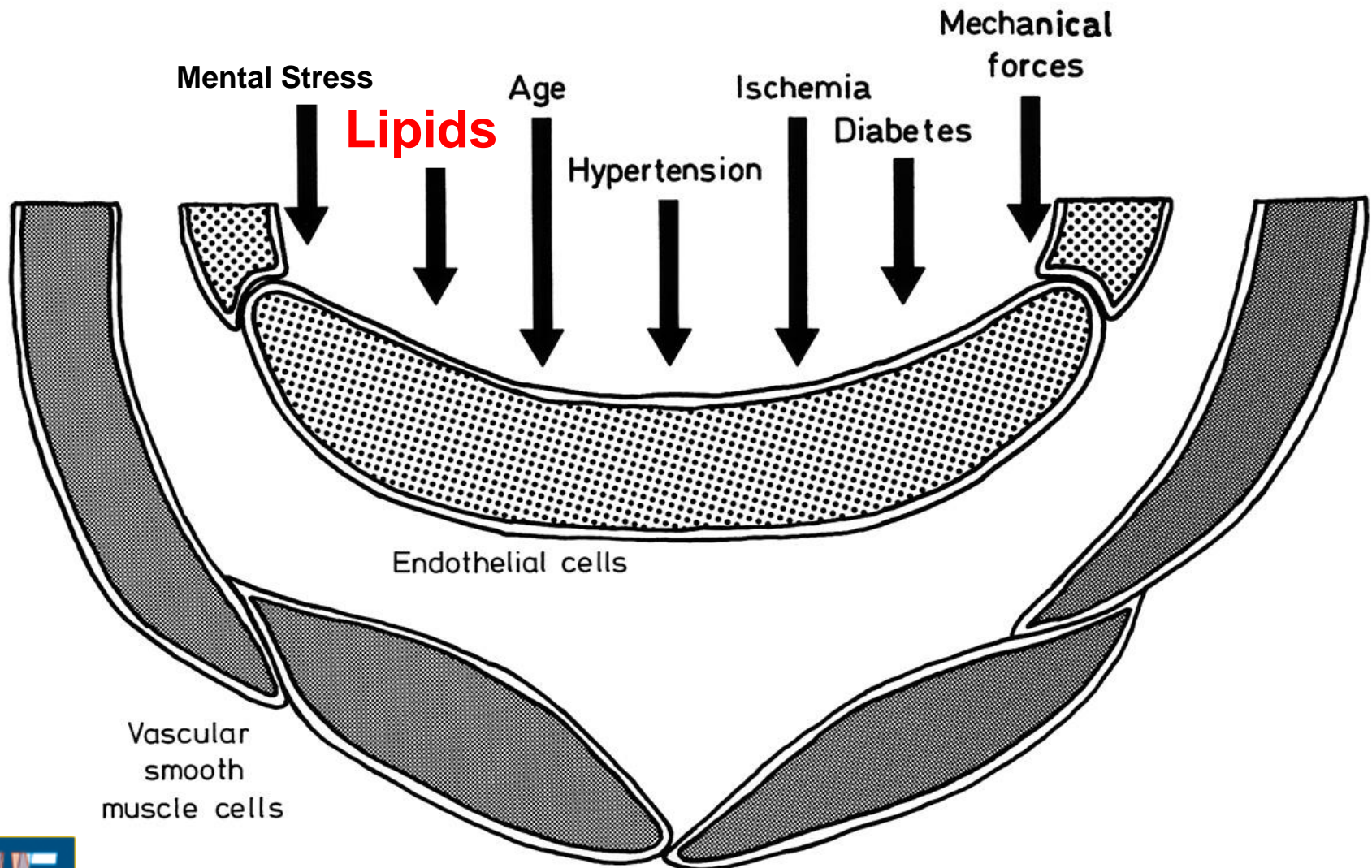
Prostanoid Release in Human Aortic Endothelial Cells

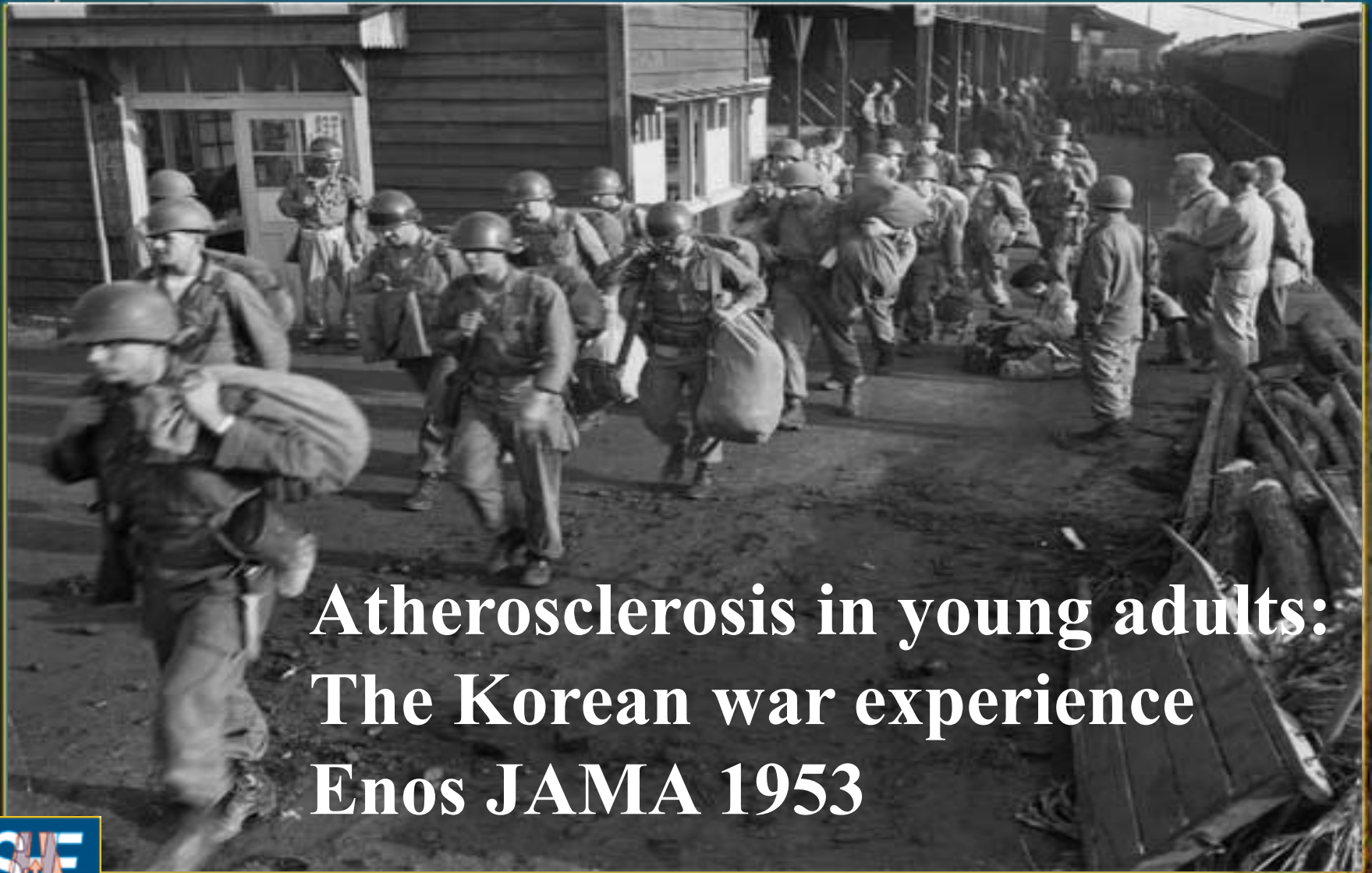


Endothelial Dysfunction in Diabetes Mellitus



Risk Factors and Endothelium Function

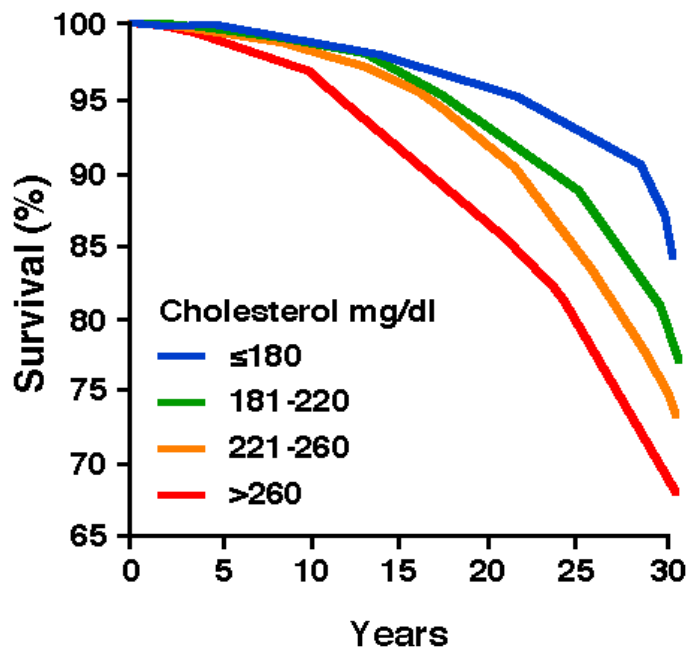




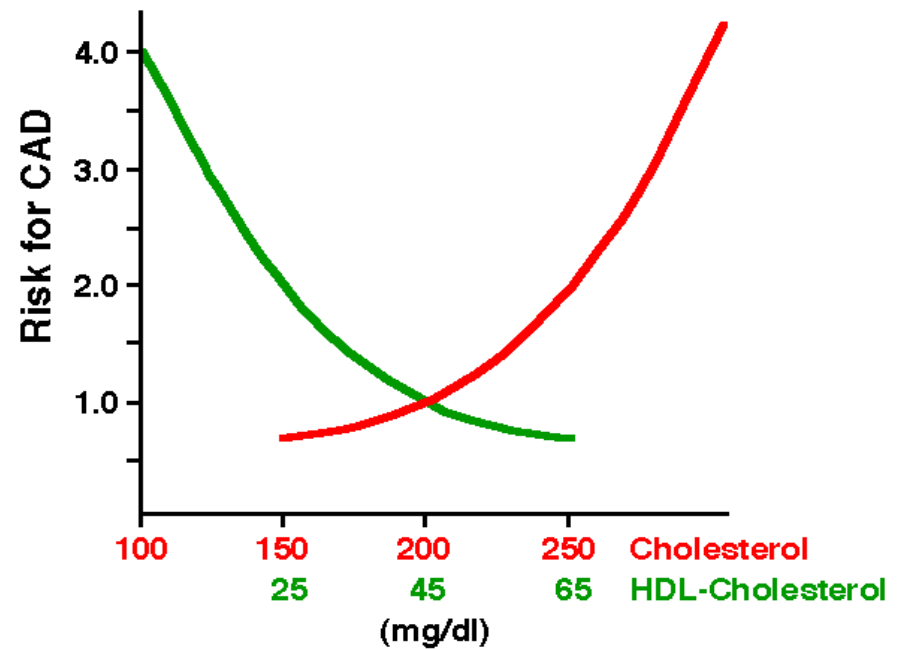
**Atherosclerosis in young adults:
The Korean war experience
Enos JAMA 1953**

Cholesterol as a Riskfactor

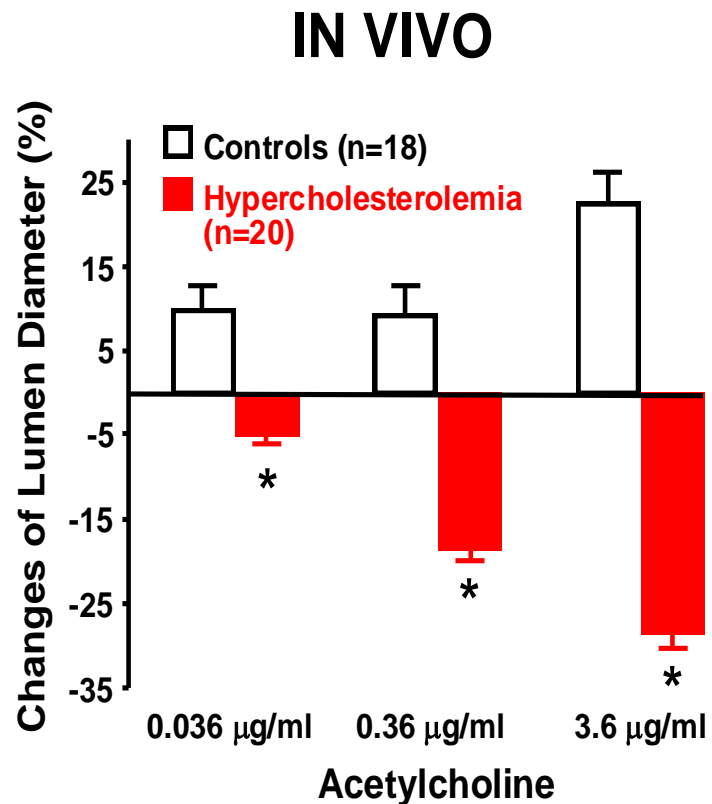
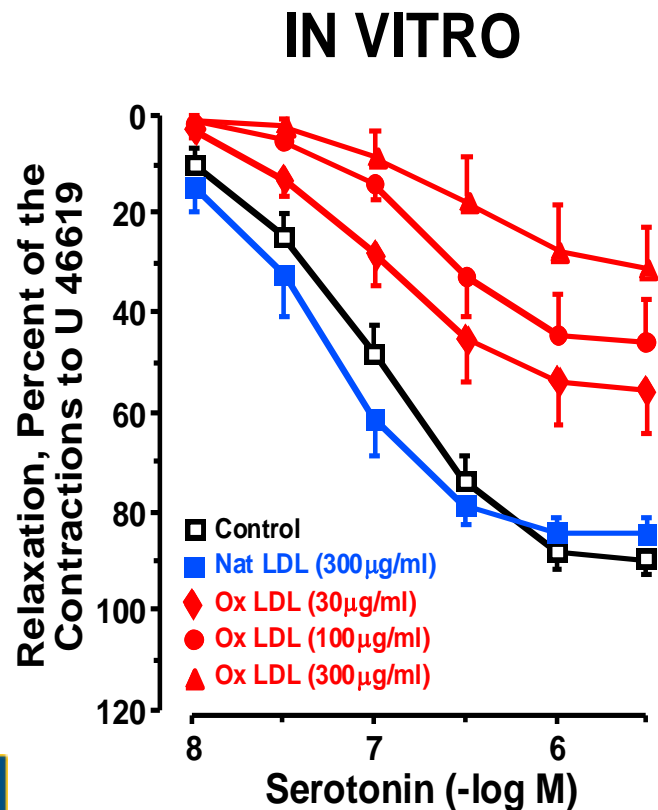
Mortality



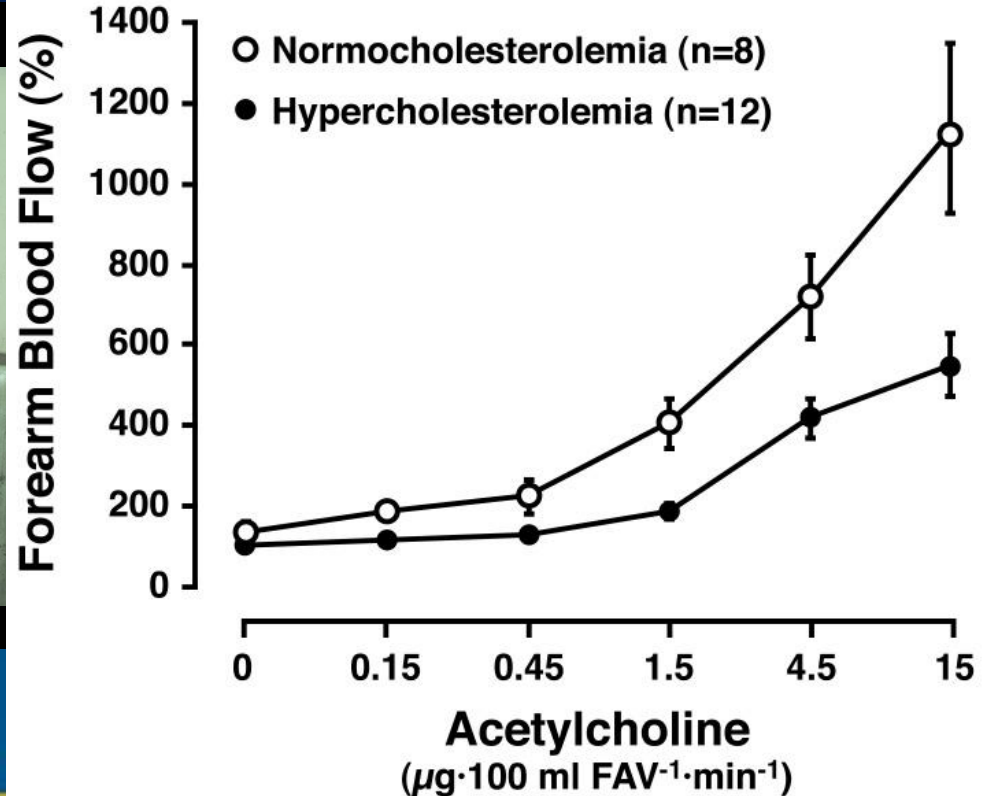
Coronary Artery Disease



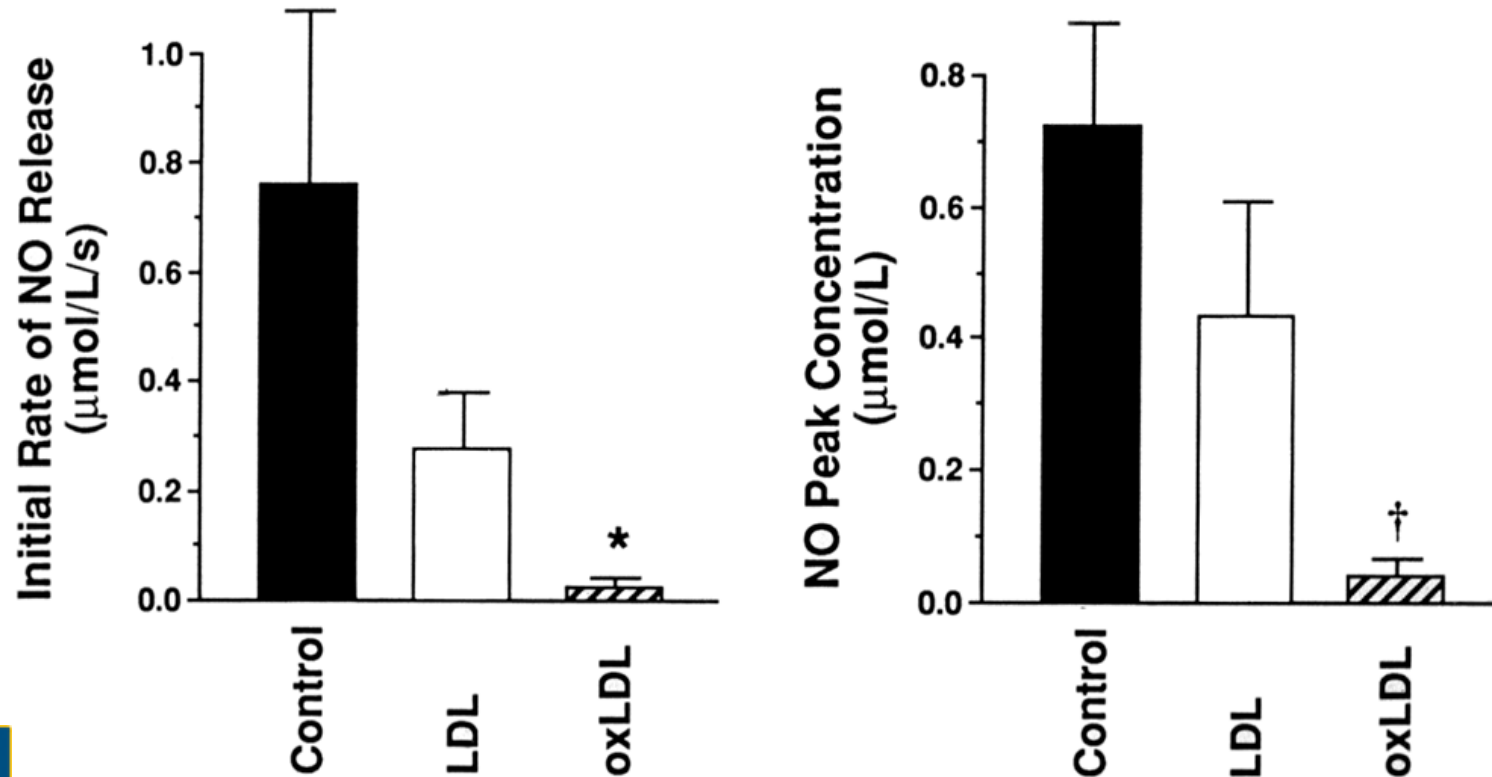
Cholesterol and Endothelial Function in Coronary Arteries



Hypercholesterolemia and Endothelial Function



Effect of Low-density Lipoprotein on NO Release in Cultured HAEC



Pathogenesis of Arteriosclerosis

