

Men, their Heart and Private Parts

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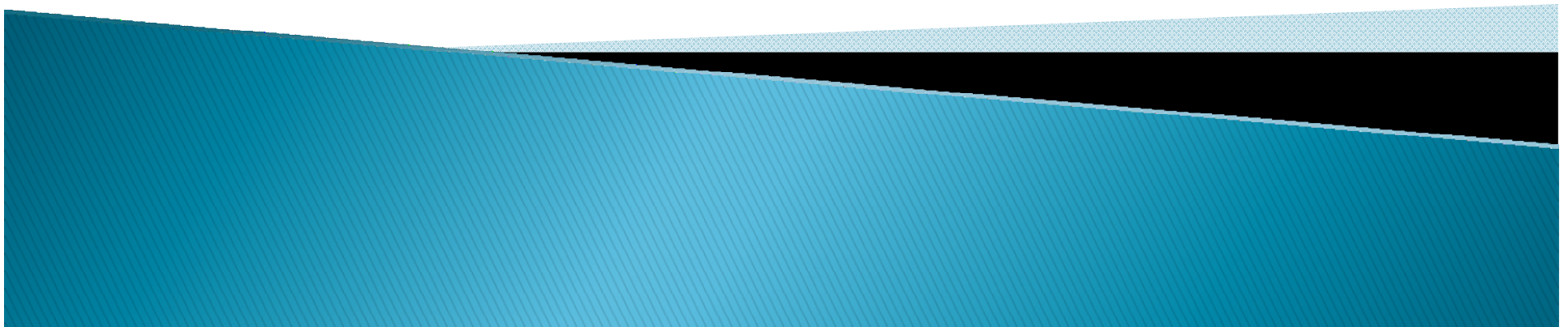
Erectile Dysfunction and Cardiovascular Disease

- Some patients develop Erectile Dysfunction before cardiovascular disease
- Could ED be a sentinel marker for cardiovascular disease?



Common Ground

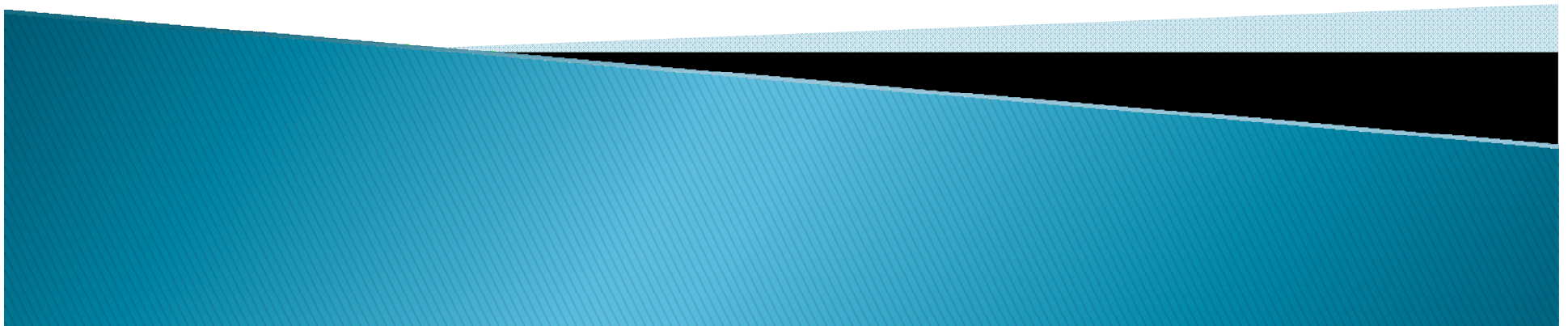
How are erectile dysfunction and cardiovascular disease related?



Shared Risk Factors

80% of ED has a vascular aetiology

- hyperlipidaemia
- hypertension
- diabetes
- smoking
- obesity/inactivity



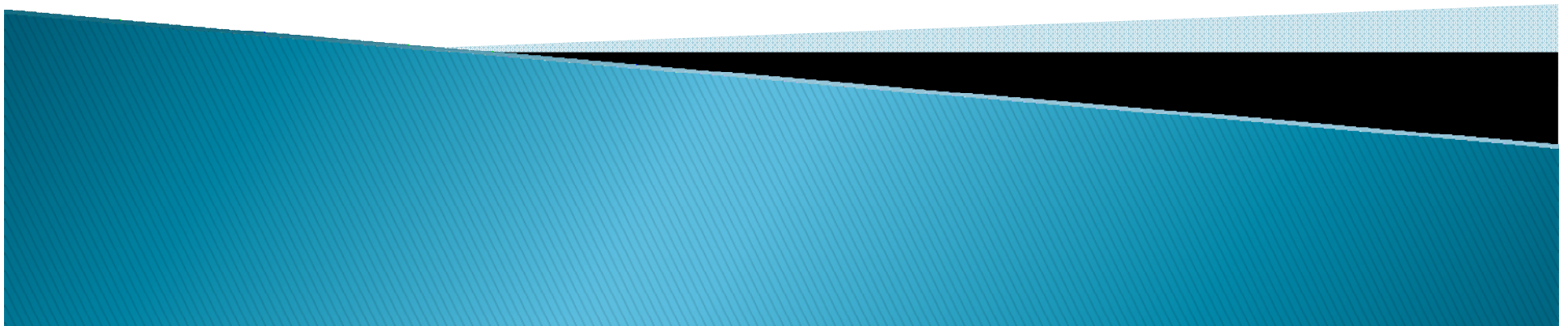
Other causes of ED



Shared Pathogenesis

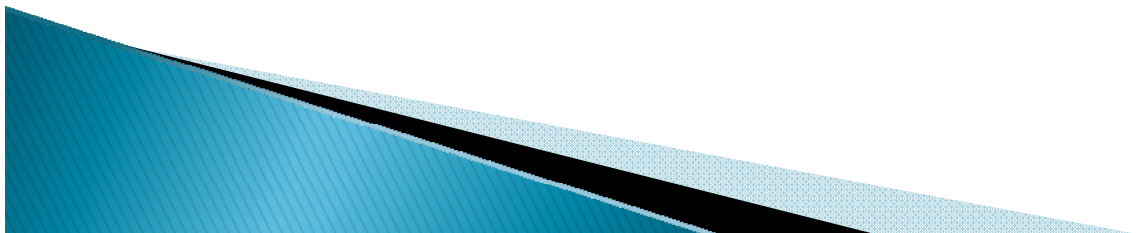
➤ Endothelial Dysfunction

➤ Atherosclerosis

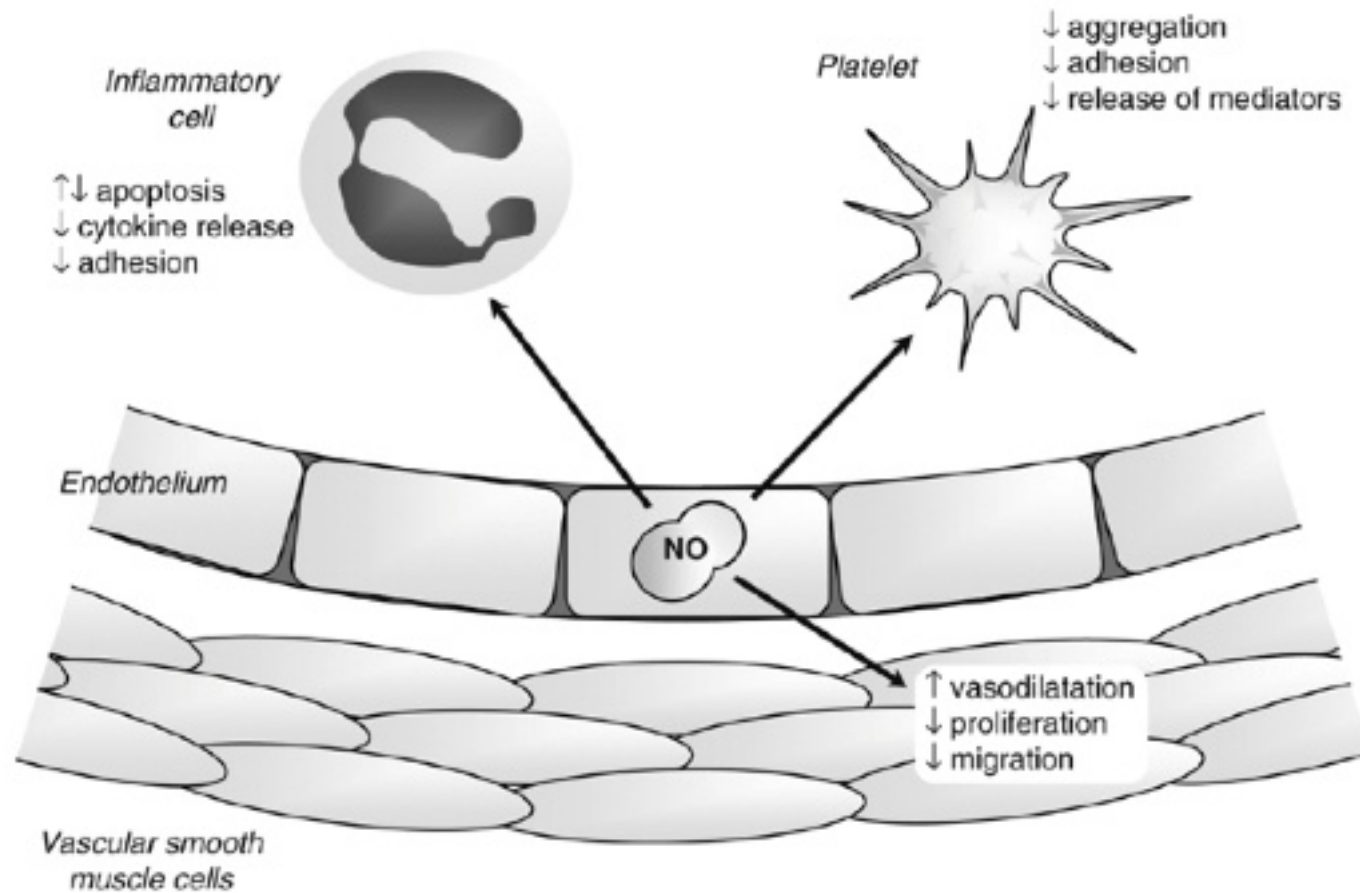


Endothelial Dysfunction

- ▶ intimately linked to atherogenesis and CV risk
- ▶ altered release of vasoactive factors
 - Nitric Oxide – parasympathetic nNO
 - endothelium eNO

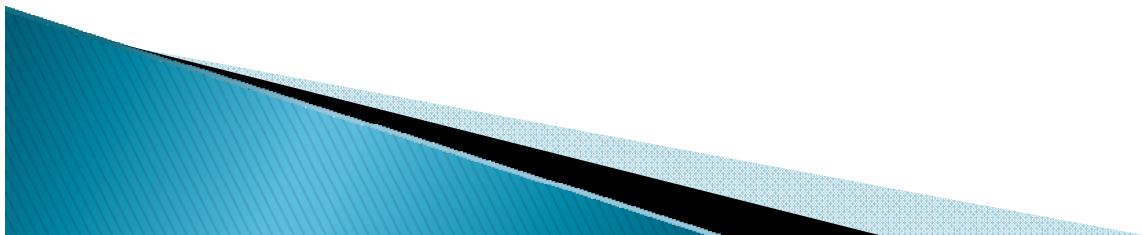


Biological Functions of Nitric Oxide



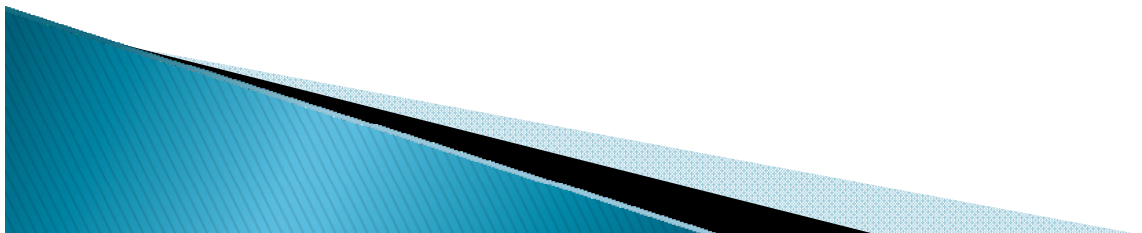
Endothelial Dysfunction

- ▶ Alteration in the release/function of NO is Atherogenic
 - vasoconstriction
 - coagulation
 - increased leucocyte adhesion
 - smooth muscle growth



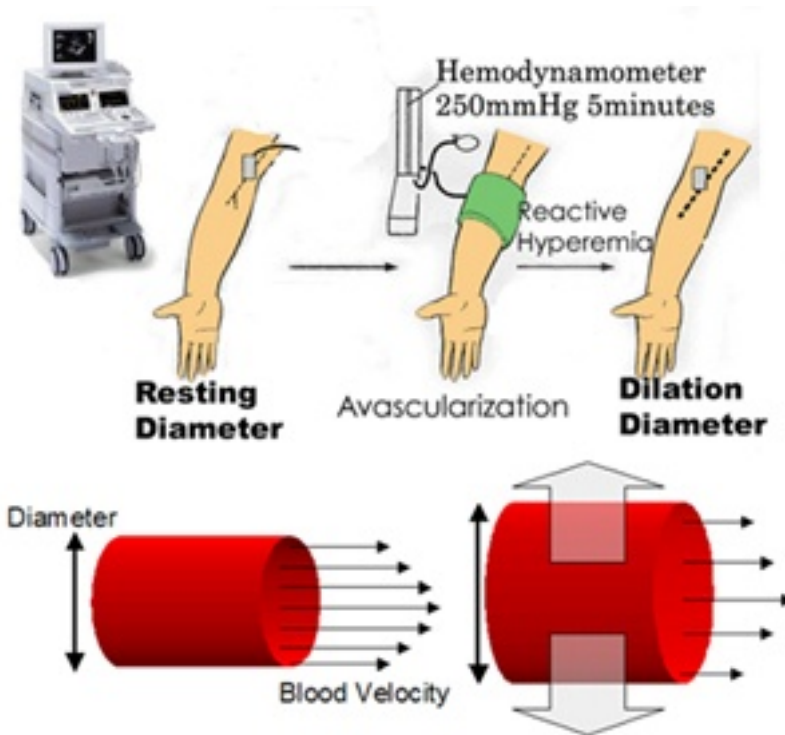
Endothelial Dysfunction

- ▶ Several risk factors for Cardiovascular disease are related to endothelial dysfunction
 - Traditional smoking, hypertension
 dyslipidaemia, diabetes
 - New inflammation, hypoxia
 oxidative stress



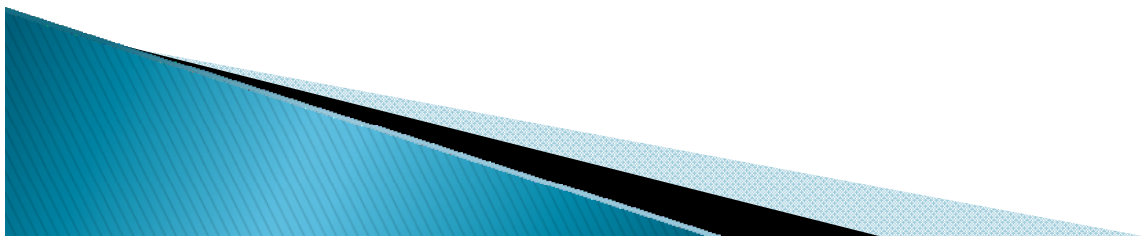
Measuring Endothelial Dysfunction

- ▶ Measure change in arterial diameter or flow
- ▶ Acetylcholine or L-arginine → eNO
- ▶ Mechanical
 - arm artery dilatation mainly NO dependent



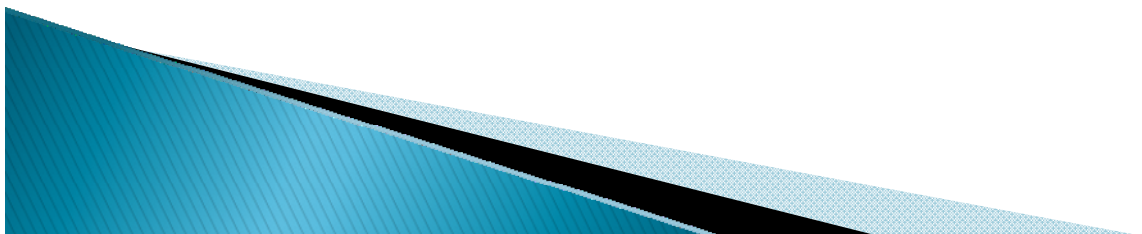
Endothelial Dysfunction

- ▶ predicts cardiovascular events
- ▶ FMD predicts coronary artery dysfunction more accurately than peripheral dysfunction
- ▶ forearm artery dilatation reflects total body NO



Endothelial Dysfunction and ED

- ▶ could ED be a marker of early endothelial dysfunction?



Endothelial Dysfunction and ED

- ▶ 41 patients with ED and no CVD
- ▶ Compared to 30 age-matched controls
- ▶ Flow mediated vasodilatation
 - brachial artery diameter pre and post occlusion
 - sensitive measure of endothelial dysfunction

Lojanapiwat et al 2009



Endothelial Dysfunction

- ▶ Groups similar apart from HDL levels
- ▶ Brachial diameter – baseline no difference
 - lower FMD in ED patients

5.1 mm vs 8.7 mm

- ▶ Endothelial Dysfunction present in ED patients without cardiovascular disease

Lojanapiwat et al 2009

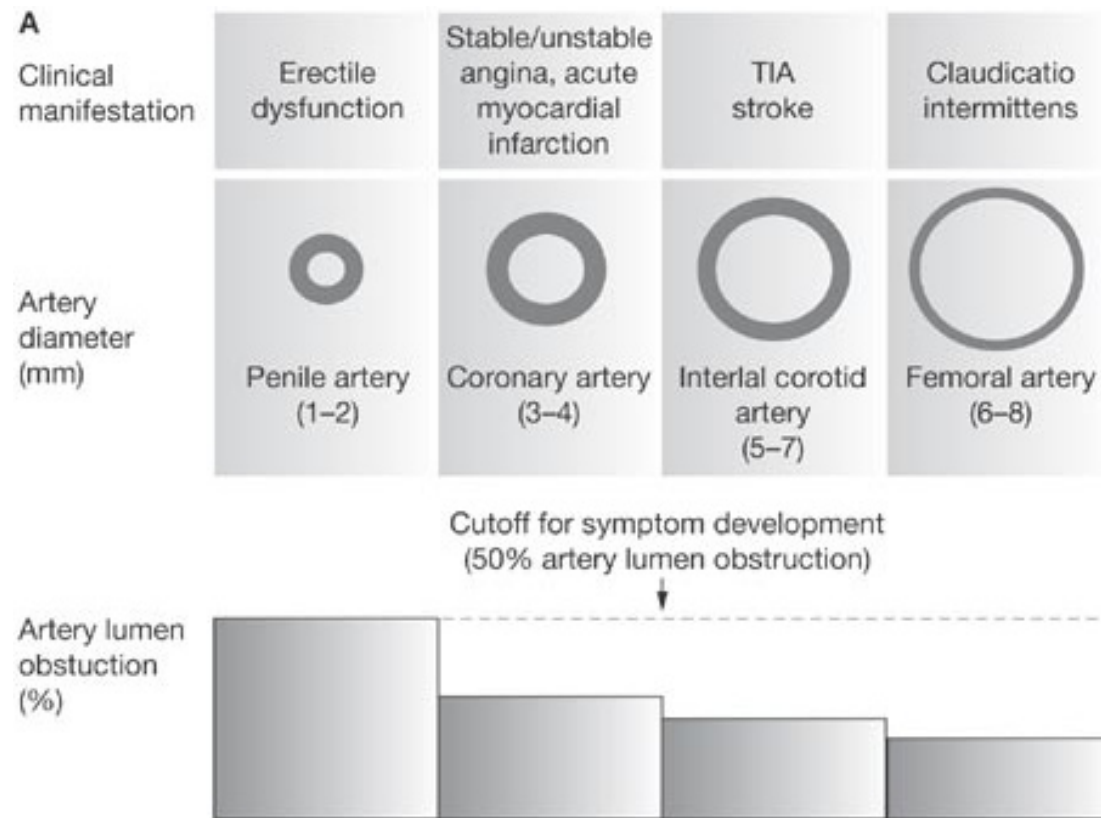


Evidence for ED predating CVD

- ▶ 300 patients with acute chest pain and coronary artery disease on angiography
- ▶ ED prevalence 49%
- ▶ ED developed before CAD in 67%
- ▶ Mean time interval 38.8 months
- ▶ All Type 1 Diabetes develop ED before CAD

Why might ED predate CAD?

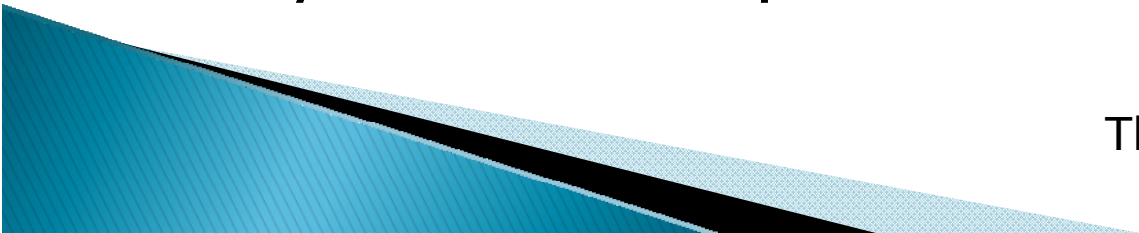
Artery Size Hypothesis



Can ED predict Cardiovascular Disease?

- ▶ Prostate Cancer Prevention Trial
- ▶ Men over 55 years, 1993–2004
- ▶ Placebo arm evaluated 3 monthly for ED and CVD
- ▶ 7 year follow-up

Thompson et al JAMA 2005



Can ED predict Cardiovascular Disease?

- ▶ 8063 had no cardiovascular disease
- ▶ 3816 (47%) has some ED
- ▶ 4247 (53%) had no ED
 - 57% developed ED at 5 years
 - 65% developed ED at 7 years

Can ED predict Cardiovascular Disease?

- ▶ Incident developed Angina HR-1.53
 - Stroke HR-1.70

- ▶ Incident or prevalent ED HR-1.45
 developed CVD
 - Angina or MI HR-1.55

 - Transient Ischaemic Attack HR-1.92

Can ED predict Cardiovascular Disease?

- ▶ The association was independent of
 - age, hypertension, diabetes
 - hyperlipidaemia, smoking
- ▶ Predictive ability of Incident ED

similar magnitude to smoking, FHx,
hyperlipidaemia

Thompson et al JAMA 2005



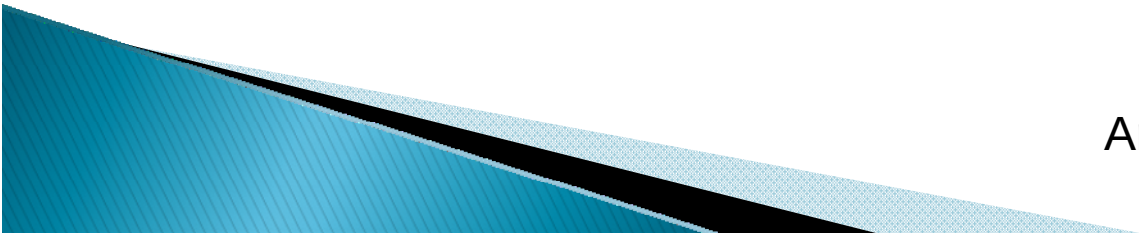
Can ED predict Cardiovascular Disease?

▶ Massachusetts Male Aging Study

- population-based, prospective study
- 1709 men 40–79 years
- 1057 free of CVD and diabetes
- 261 cases of CVD over 10 years

- Erectile Dysfunction HR– 1.42
- Traditional risk factors HR– 1.41

Araujo et al J Urology 2010



Can ED predict Cardiovascular Disease?

▶ Diabetes

- Type II 2306 patients with no clinical Coronary Heart Disease followed for 4 years

ED an independent predictor of CHD HR=1.58

Ma et al JACC 2008

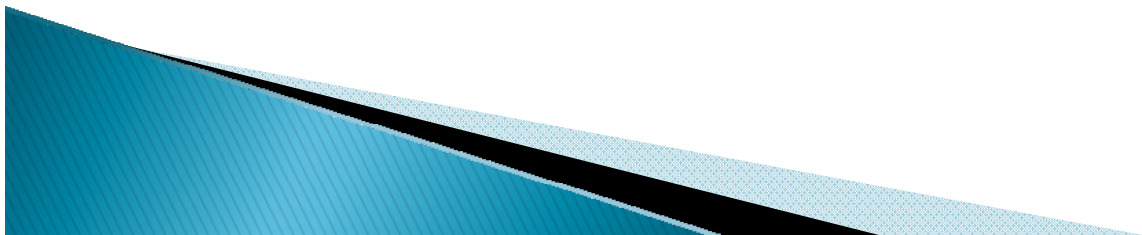
291 patients with silent CAD 4 year study
Major cardiac event in ED 61.2%, no ED 36.4%

Gazzaruso et al JACC 2008



ED predicts Cardiovascular Disease

- ▶ ED appears to be a significant independent predictor of coronary events
- ▶ Artery size hypothesis or some other unknown link?

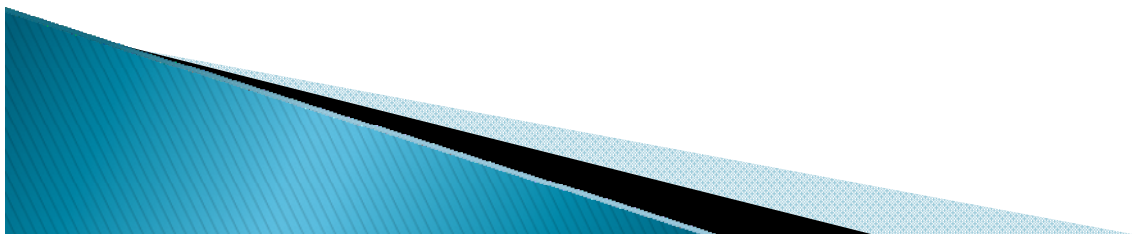


Can ED predict Cardiovascular morbidity and mortality?

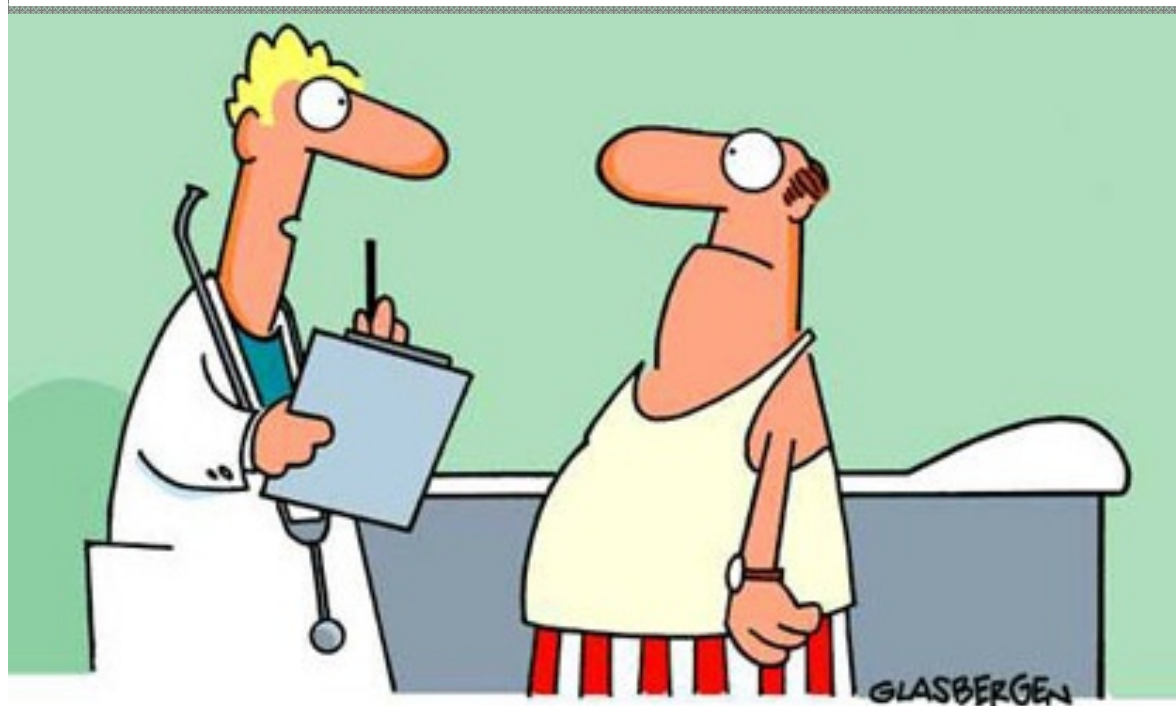
- ▶ High Risk patients with Cardiovascular disease
- ▶ Double blind randomisation ACE and ARB
 - Ramipril, Telmisartan or both (ONTARGET)
 - Telmisartan or placebo (TRANSCEND)
 - ED predicts
 - all cause death HR– 1.84
 - cardiovascular death HR– 1.93
 - myocardial infarction HR– 2.02

Are Erectile and Endothelial Dysfunction reversible?

- ▶ Lifestyle modification
 - diet
 - exercise
- ▶ Cardiovascular drugs
- ▶ PDE-5 inhibitors



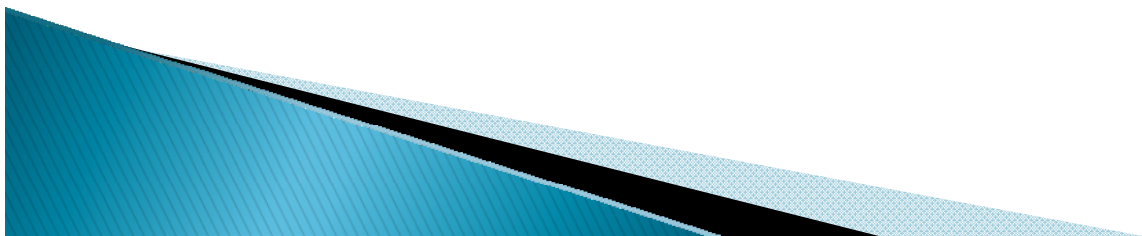
Lifestyle modifications



“What fits your busy schedule better, exercising one hour a day or being dead 24 hours a day?”

Lifestyle modifications

- ▶ Animal studies
 - age-related decline in erectile function
 - reversed by exercise and caloric restriction
 - body weight did not have to fall
 - older and hypertensive rats are more sensitive to caloric intake, weight gain, exercise



Lifestyle modifications

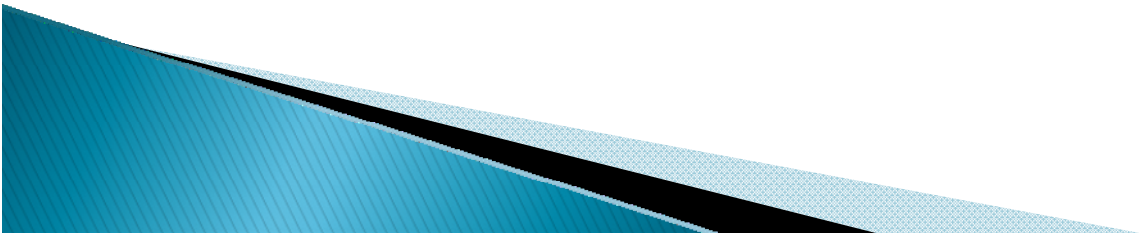
▶ Human studies

- Exercise
 - vigorous vs walking
 - improved erections

White et al Arch Sex Behav 1990

- Diet
 - randomised controlled trial
 - 110 obese men with ED
 - no diabetes, hypertension, CVD
 - individualised diet and exercise vs advice about healthy food/exercise

Esposito et al JAMA 2004



Lifestyle modifications

▶ Human studies

- Diet – aim for 10% reduction in weight

- results
 - healthier diet
 - 48 min/wk exercise vs 36
 - 15 vs 2 kg reduction
 - reduced BP
 - cholesterol
 - glucose
 - IL-6,8 CRP
 - L-Arginine response
 - 3 point IIEF increase vs 0.1

Esposito et al JAMA 2004

Lifestyle modifications

▶ Human studies

- Diet
 - Mediterranean diet vs healthy info
 - walking 30 min/day for both groups
 - 65 men with the metabolic syndrome
35 to diet, 30 to advice
 - decreased glucose, BP, LDL cholesterol
 - improved endothelial function score
 - IIEF change 3.7 vs 0.3
 - 37% vs 7% regain normal erectile function

Cardiovascular Drugs



"Discouraging data on the antidepressant."

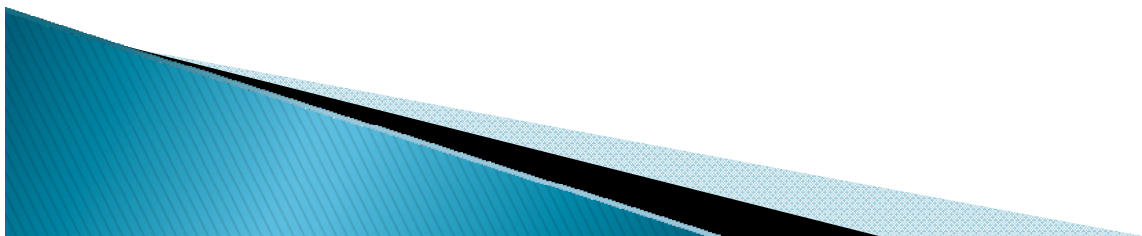
Cardiovascular Drugs

- ▶ Double blind randomisation ACE and ARB
 - Ramipril, Telmisartan or both (ONTARGET)
 - Telmisartan or placebo (TRANSCEND)
 - did not improve or worsen ED
 - Statins, B Blockers no benefit except Sildenafil + Atorvastatin vs Sildenafil



PDE-5 Inhibitors

- ▶ Tadalafil and Sildenafil improve endothelial function in men at increased risk of CVD
- ▶ Similar findings in diabetics with Sildenafil
- ▶ Effect evident in different vascular beds
- ▶ Reduction in inflammatory markers



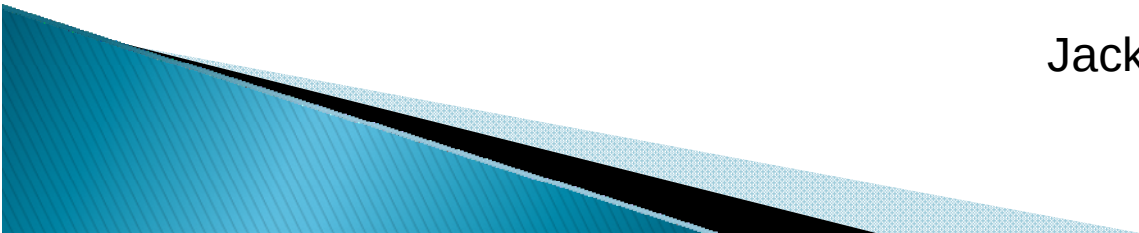
Princeton Consensus

▶ Erectile Dysfunction and Cardiology

1999 and 2006

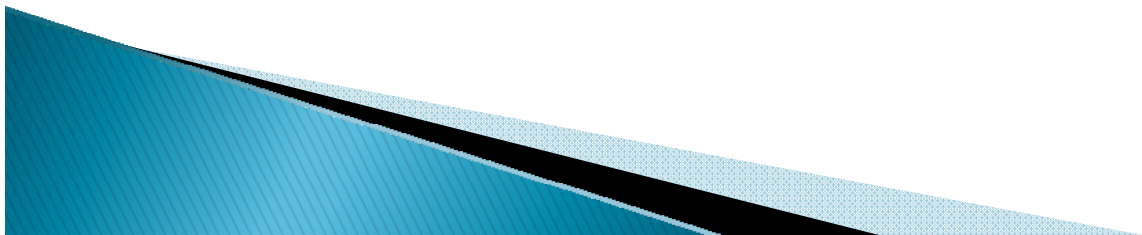
- endothelial dysfunction is a common denominator for ED and CVD
- any asymptomatic man with ED should have lipids, glucose, BP and ideally an exercise ECG
- lifestyle intervention (weight loss and exercise) should be encouraged

Jackson G et al J Sex Med 2006



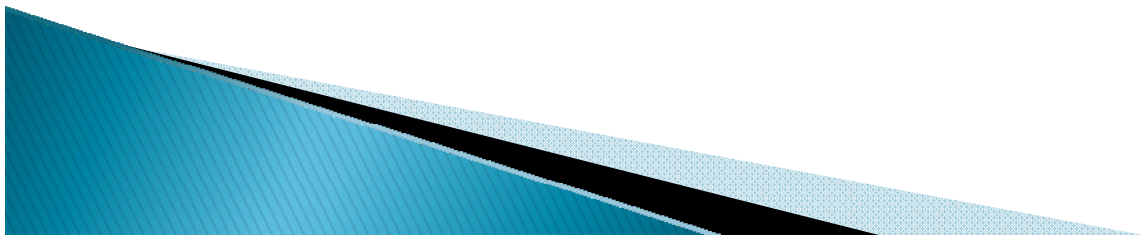
Conclusions

- ▶ Erectile and endothelial dysfunction co-exist in those with CVD
- ▶ Erectile and endothelial dysfunction are linked by abnormalities in the Nitric oxide pathway
- ▶ Erectile dysfunction predates cardiovascular disease by 3 years in 2/3 of patients



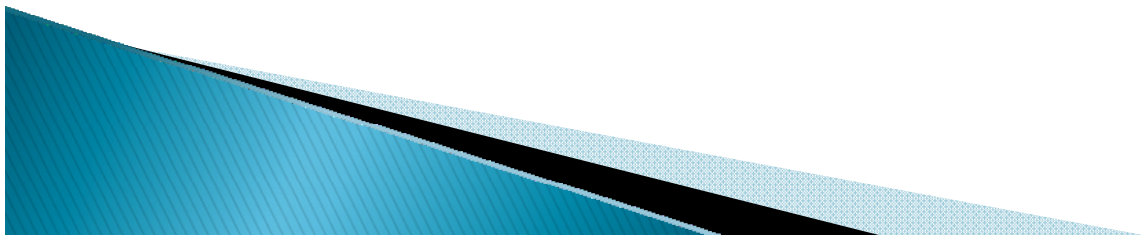
Conclusions

- ▶ Erectile dysfunction is an independent predictor of CVD similar to other risk factors
- ▶ Erectile dysfunction is a potent predictor of CVD mortality
- ▶ Patients with erectile dysfunction and no cardiac symptoms are a cardiac patient until proven otherwise – these patients warrant investigation and advice



Conclusions

- ▶ Diabetics with ED may warrant screening for silent coronary artery disease
- ▶ Lifestyle modifications can reverse erectile dysfunction in the obese and those with the metabolic syndrome
- ▶ PDE-5 inhibitors can improve both Erectile and endothelial dysfunction





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**“Yes, that was very loud, but I said
I wanted to hear your HEART!”**

Endothelial Dysfunction

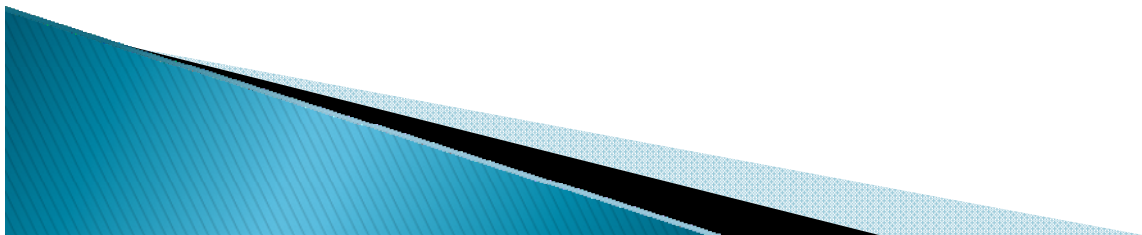
- ▶ Nitric Oxide

- subluminal vasodilator

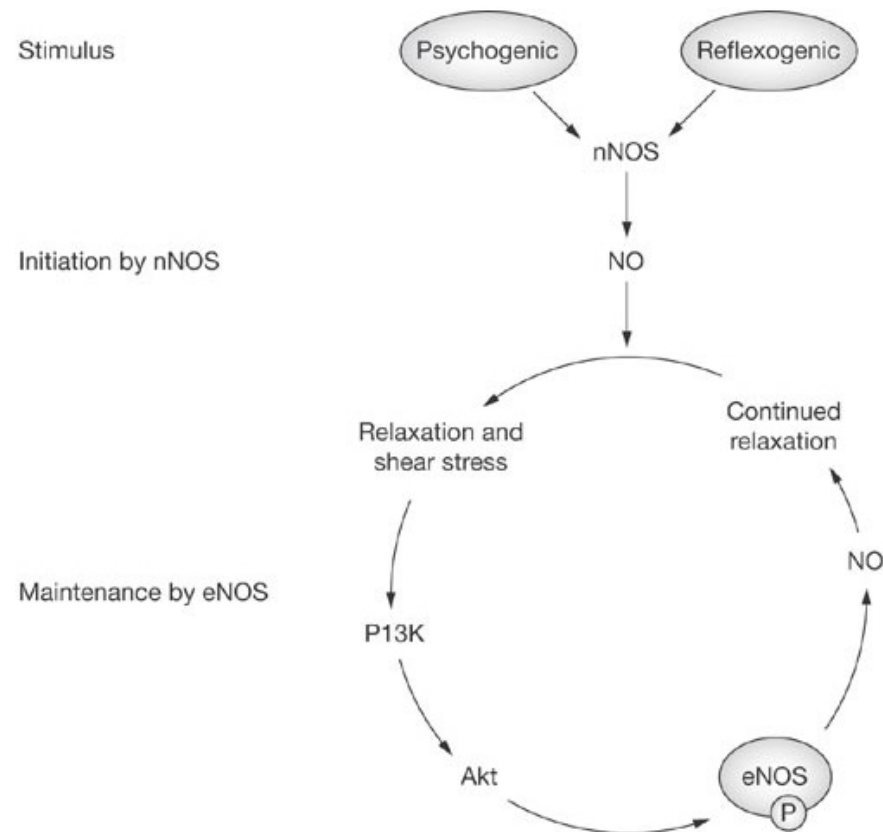
- antiproliferative

- intaluminal

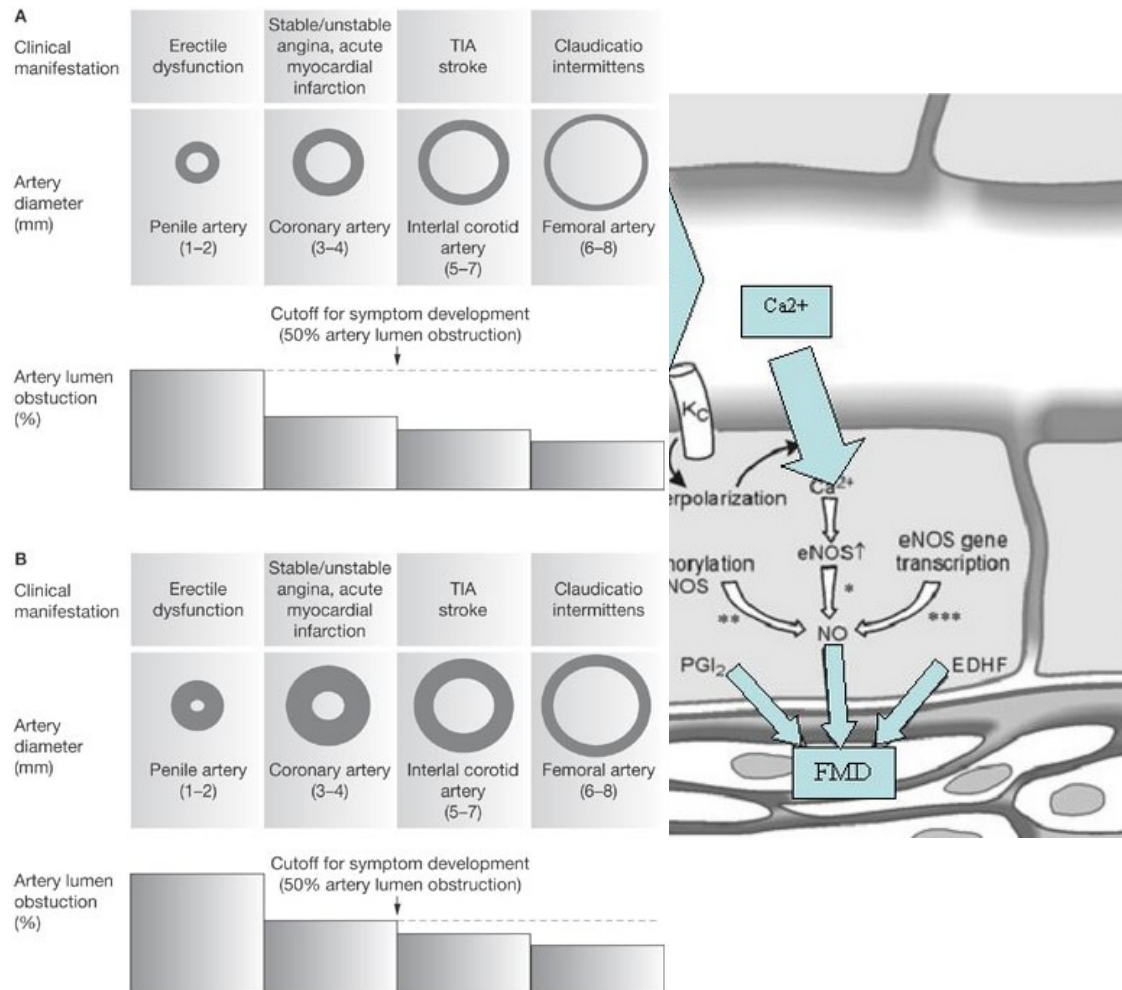
- anticoagulant
antiadhesive
antiplatelet



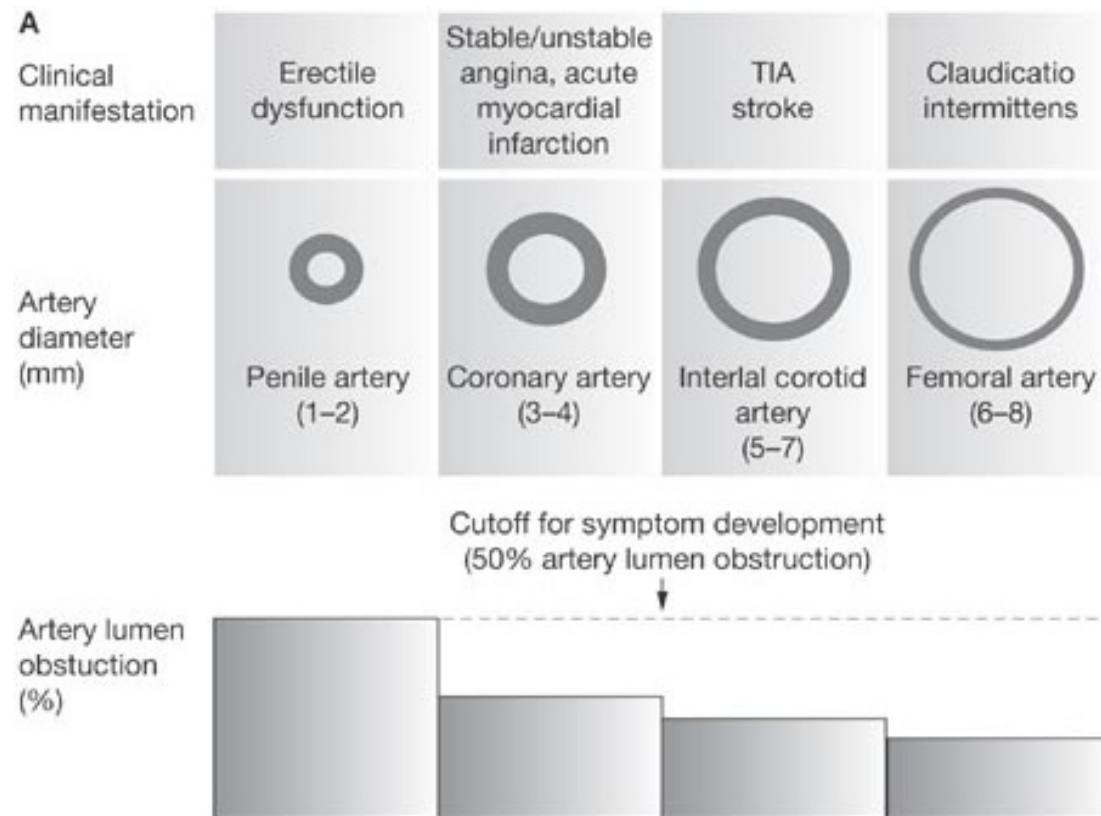
Endothelial Dysfunction



eNOS
Endothelium of vessels
and vascular sinusoids



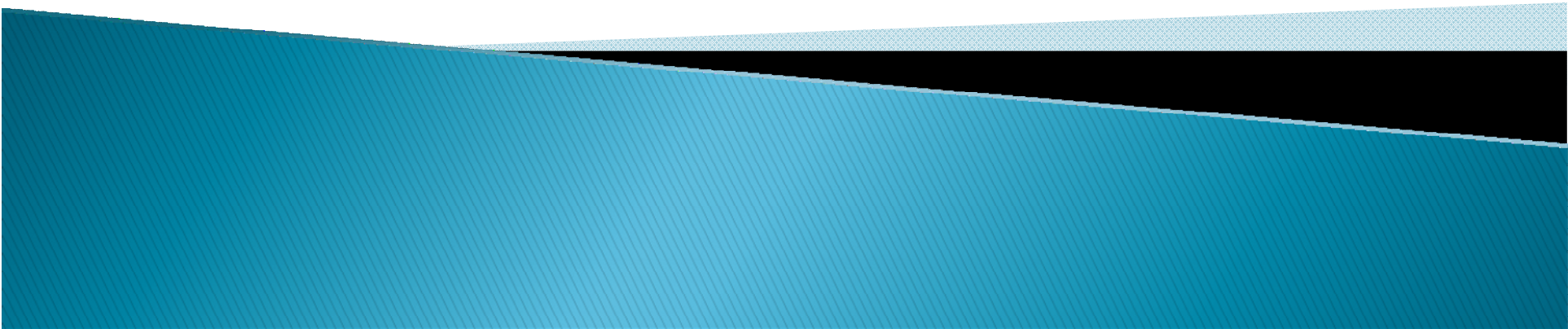
Why might ED present earlier?

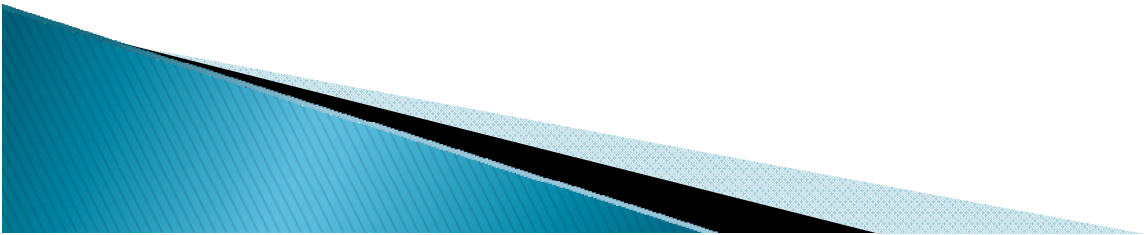


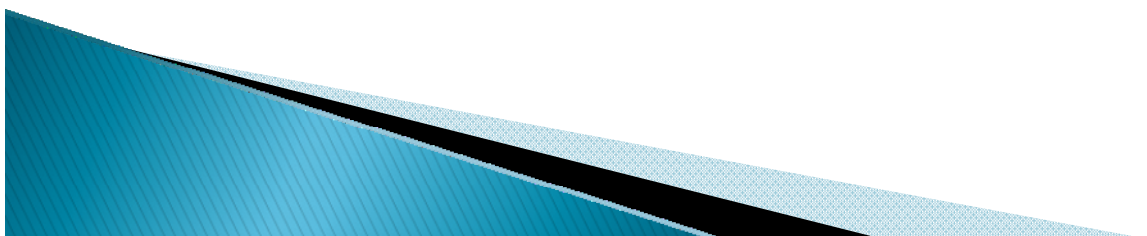


“What fits your busy schedule better, exercising one hour a day or being dead 24 hours a day?”

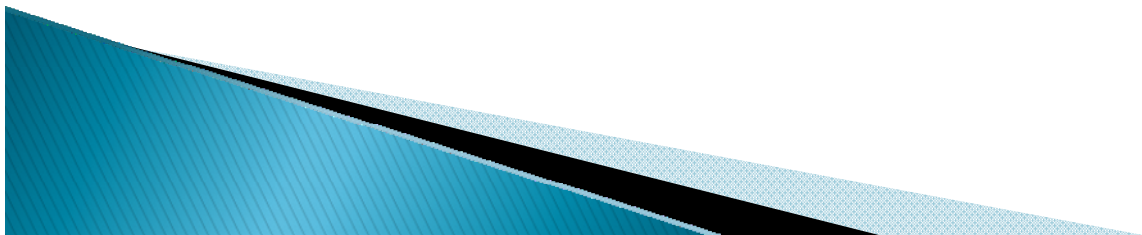
»» This one is good







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