PLAC™ Test

WHEN PLAQUE ATTACKS!!

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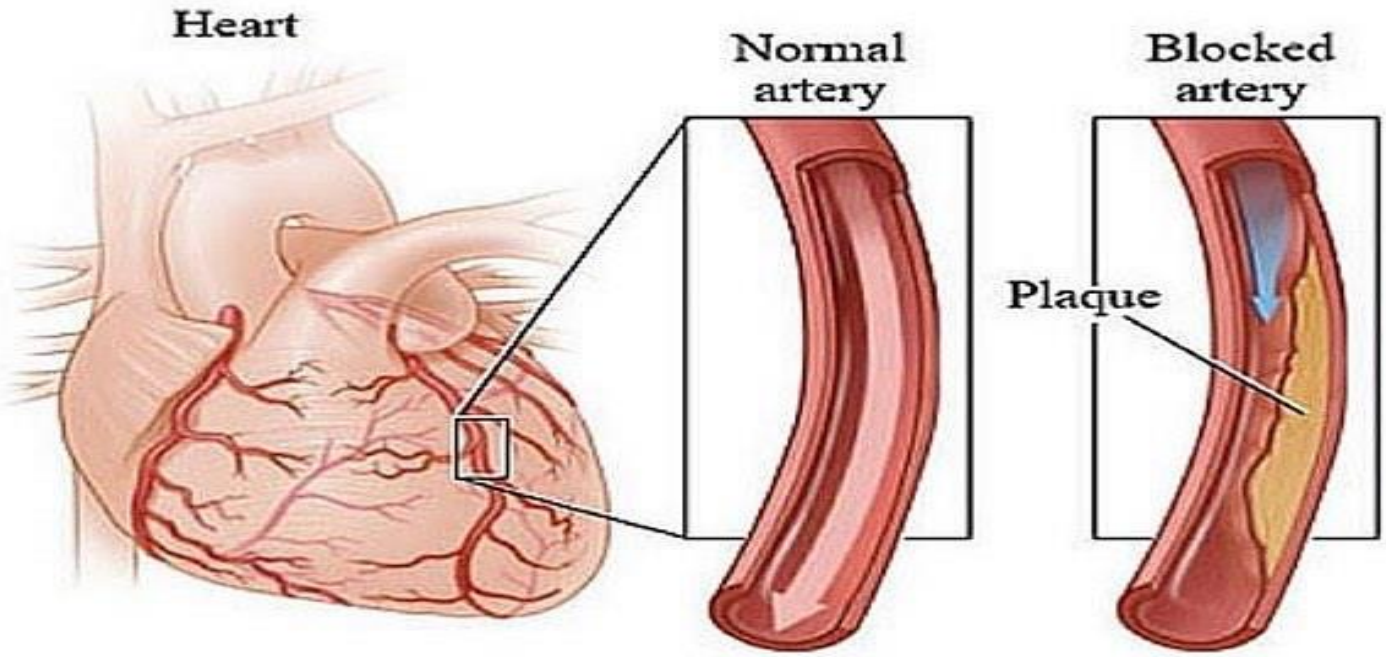
KEEP MAKING THOSE BACON JOKES



...WHILE YOU STILL CAN!

WHAT IS THE PLAC™ TEST

- Test cleared by the FDA to predict hidden risks of CHD
- Manufactured by diaDexus, Inc.
- Used to measure the biomarker Lp-PLA2
  - Improve preventative
  - Reduce CHD-related mortality
- Two Versions of PLAC Test
  - PLAC ELISA Test
  - PLAC Activity Test

PLAC™ TEST

PRINCIPLES

- Measures lipoprotein-associated phospholipase A_2 (Lp-PLA_2)
- Lp-PLA_2 is independent of other cardiovascular risk factors
- Lp-PLA_2 is made in artherosclerotic plaque
  - Acts as a specific marker for inflammation
  - Directly involved in formation of rupture prone plaque
- Inexpensive, minimal risk, and convenient

METHODS

- Sandwich immunoassay that uses two highly specific monoclonal antibodies
  - Directly measures concentration in serum and plasma
- Incubated with immobilized monoclonal antibody (2C10) against Lp-PLA_2
  - 96 well microtiter plate
- Identified by a second monoclonal anti-Lp-PLA_2 antibody (4B4) labeled with horseradish peroxidase

CLINICAL APPLICATIONS

- Lp-PLA_2 is the biomarker used to:
  - Identify persons at increased risk for CHD events
  - Predict novel risk of CHD in patients with no prior history of cardiovascular events
  - Obtain a prognostic value independent of standard lipid profile testing
  - Use in conjunction with clinical evaluation and patient risk assessment

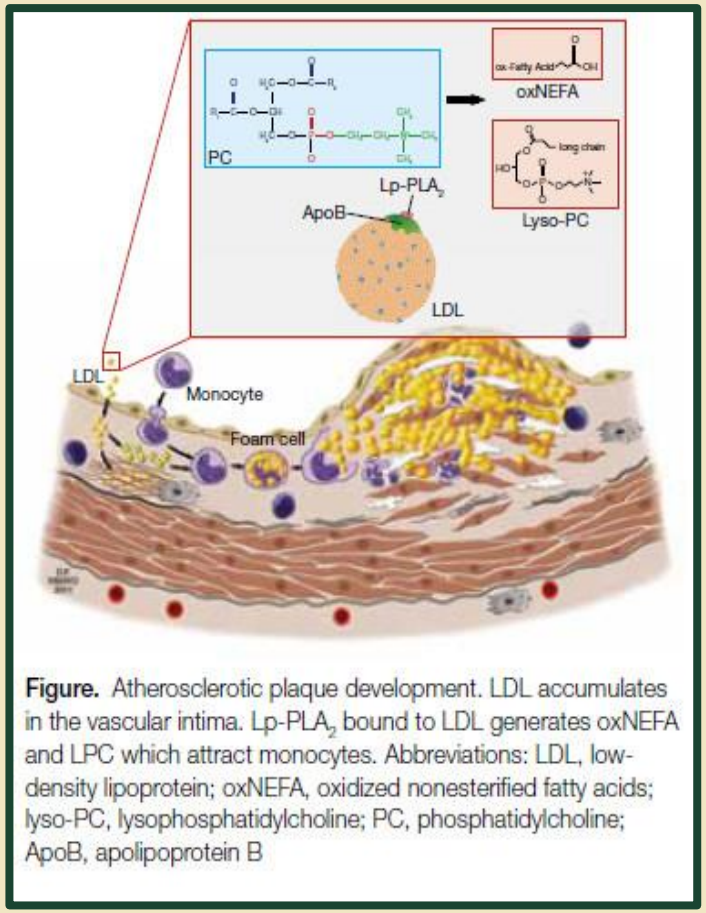
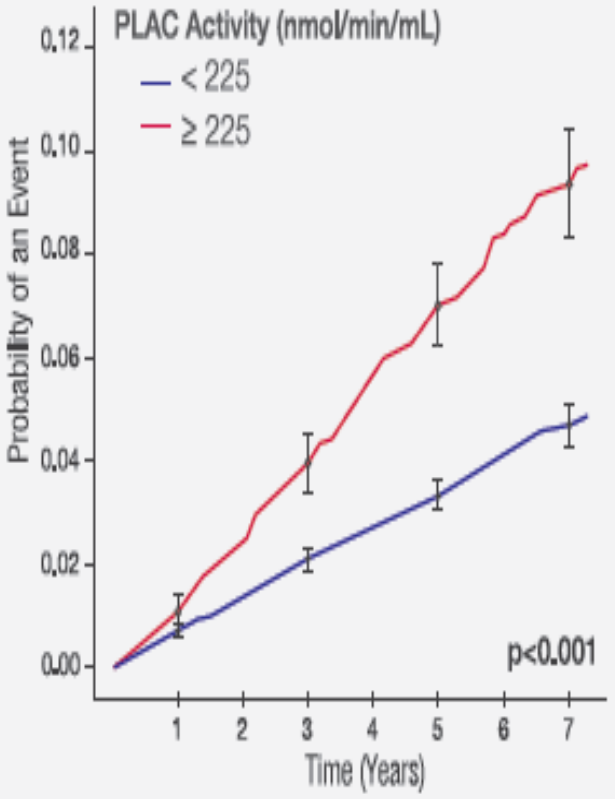


Figure. Atherosclerotic plaque development. LDL accumulates in the vascular intima. Lp-PLA_2 bound to LDL generates oxNEFA and LPC which attract monocytes. Abbreviations: LDL, low-density lipoprotein; oxNEFA, oxidized nonesterified fatty acids; lyso-PC, lysophosphatidylcholine; PC, phosphatidylcholine; ApoB, apolipoprotein B

RISK RANGES FOR Lp-PLA_2

HIGH RISK	MODERATE RISK	LOW RISK
>235 ng/mL	**200-235 ng/mL**	**<200 ng/mL**
▯ Therapeutic lifestyle changes ▯ Plasma glucose <110 mg/dL ▯ Systolic bp <120 mmHg and diastolic <80 mmHg to reduce CV risk associated with hypertension ▯ LDL <100 mg/dL ▯ Appropriate drug treatment	▯ Evaluate other risk factors and consider more aggressive management if necessary ▯ Consider therapeutic lifestyle changes	▯ Encourage patients to maintain a healthy lifestyle ▯ Continue to monitor as appropriate

Total CHD Event Rates[4]



PLAC Activity Prediction of CHD Events[4]

	p value
Composite of All Three CHD Events	< 0.001
Myocardial Infarction	< 0.001
Cardiac Revascularization	< 0.001
Cardiac Mortality	< 0.001

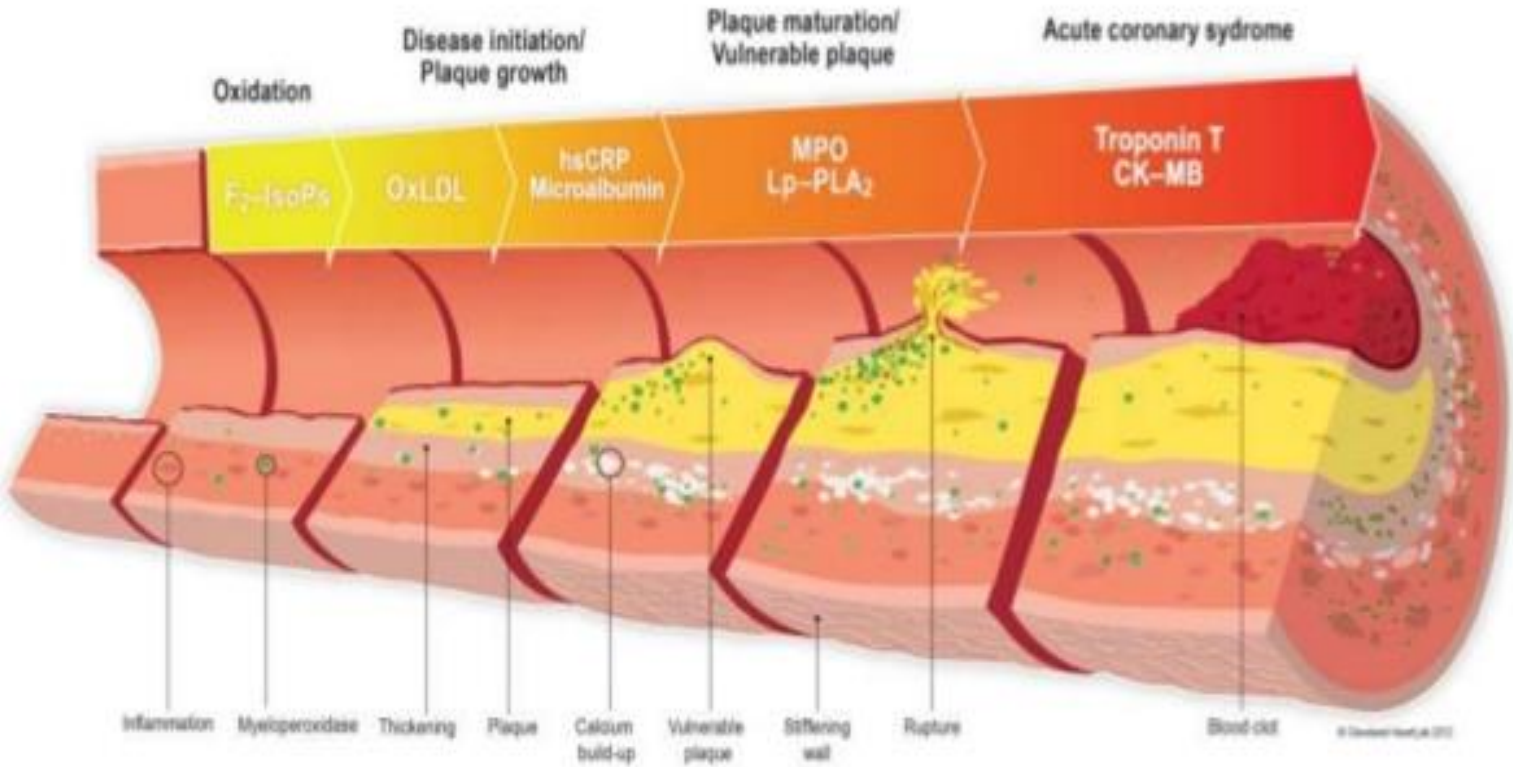
PLAC ELISA vs PLAC ACTIVITY

PLAC ELISA

- What is measured?
  - Lp-PLA_2 concentration
- Sample:
  - S or P
- FDA approval:
  - 2005
- Method:
  - Antigen-antibody interaction
- Interferences:
  - Lot variations
  - Sample stability

PLAC Activity

- What is measured?
  - Lp-PLA_2 activity
- Sample:
  - S or P
- FDA approval:
  - 2014
- Method:
  - Colorimetric
- Interferences:
  - Less interferences


Oxidation
Disease initiation/
Plaque growth
Plaque maturation/
Vulnerable plaque
Acute coronary sydrome
F2-IsoPs
OxLDL
hsCRP
Microalbumin
MPO
Lp-PLA2
Troponin T
CK-MB
Inflammation
Myeloperoxidase
Thickening
Plaque
Calcium
build-up
Vulnerable
plaque
Stiffening
wall
Rupture
Blood clot

PLAC™ TEST vs hs-CRP

Lp-PLA$_2$

- Marker of vascular inflammation
- An enzyme produced by inflammatory cells
- Involved in initiation of the early stage of vascular inflammation
- Minimal bio-variability
- Less affected by systemic inflammation

hs-CRP

- Marker of systemic inflammation
- Acute phase reactant produced by liver in response to inflammation
- May enhance the late stage of plaque progression resulting in plaque instability
- Most useful in healthy people

PLAC™ TEST ADVANTAGES

- The PLAC™ Test identifies individuals who are at an increased risk of a heart attack or stroke over traditional methods
- The PLAC™ Test is the only FDA-cleared blood test for assessing heart attack
- Non-invasive
- Less expensive
- Lp-PLA_2 is a direct measure of the status of the artery wall health unlike lipid levels

PLAC™ TEST DISADVANTAGES

- Newer method that is understudied
- It is unknown how useful the test is in those individuals who receive various treatments and interventions
  - Type 2 diabetes
  - Hypertension
  - Coronary heart disease
- More studies are needed to assess how often the PLAC™ Test should be done
- The test should not replace traditional risk factors, but to be used in conjunction

PLAC™ TEST CURRENT STATE

- Approved by the FDA
- Studies being done to confirm sensitivity and specificity
- Slowly being adopted in some labs
  - Not widespread
- Currently awaiting additional funding to continue research

REFERENCES

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QUESTIONS??