Part 1: Epidemiology of Vascular Dysfunction (Kim Sutton-Tyrrell)

- What *epidemiological data or clues exist to explain changes in vascular disease frequency* as a function of perimenopausal change?

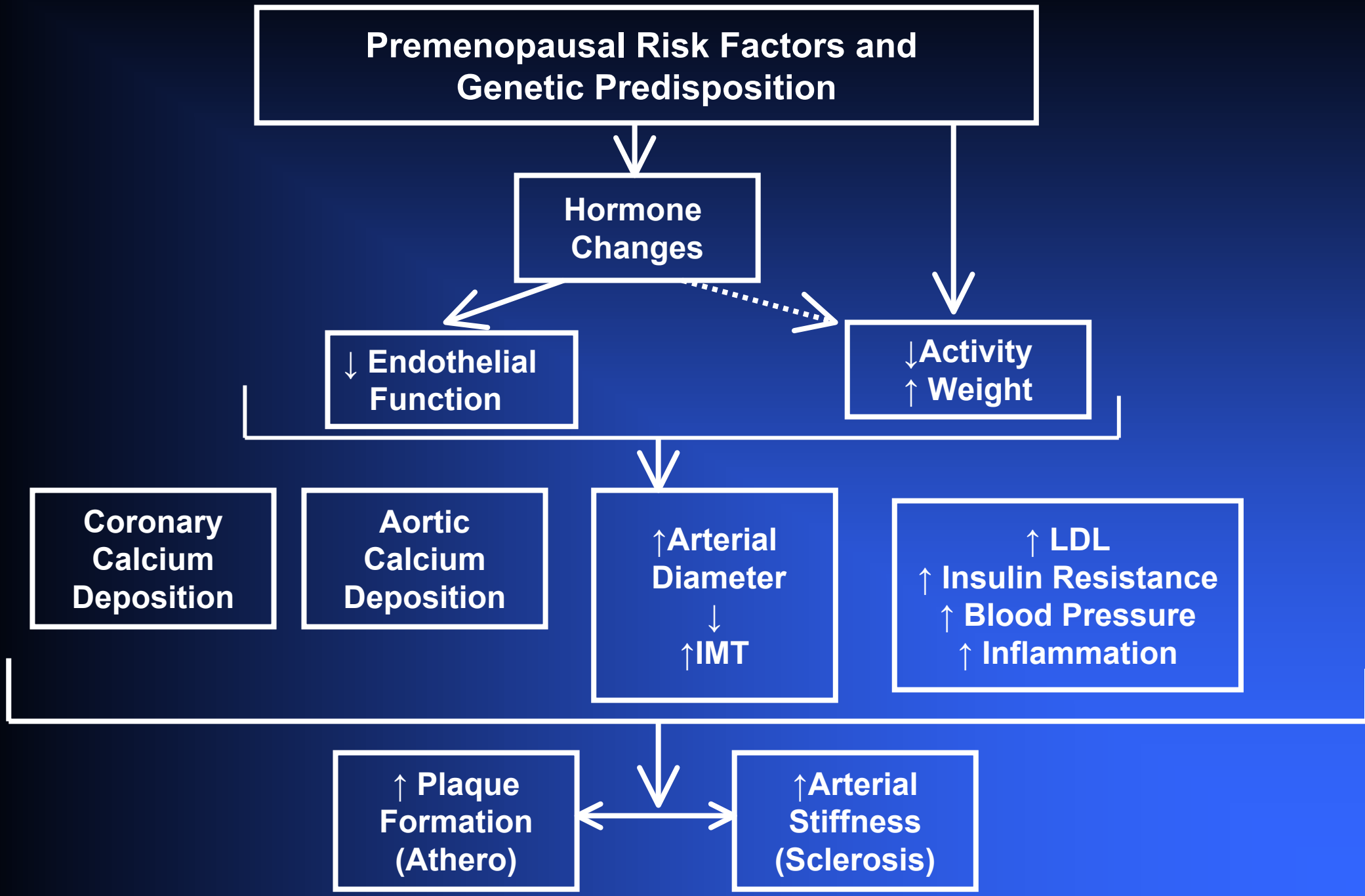
- What *epidemiological data exist regarding changes in the H-P-O axis hormones across the menopausal transition?*

What We Know – Subclincal Measures

- Menopause is associated with
  - Thicker carotid walls
  - Stiffer arteries
  - Reduced endothelial function
- Observational and Randomized HRT Use
  - Protective for Subclinical Disease
- Low T correlates with thicker carotid walls
- Low SHBG correlates with CV risk factors and thicker carotid walls
- Estrogen administration
  - Improves endothelial function
  - Has a positive inotropic effect

Areas to Explore

- Look Beyond Estrogen
  - Testosterone and other androgens
  - SHBG
  - Relative balance between androgens and estrogens
- All vessels are not equal. A given hormone likely effects different vessels differently.
- Interactions with age or duration of menopause
- Vascular Remodeling
  - Healthy, e.g. pregnancy
  - Unhealthy, eg. Vascular aging


Premenopausal Risk Factors and Genetic Predisposition
Hormone Changes
↓ Endothelial Function
↓Activity
↑ Weight
Coronary Calcium Deposition
Aortic Calcium Deposition
↑Arterial Diameter
↓
↑IMT
↑ LDL
↑ Insulin Resistance
↑ Blood Pressure
↑ Inflammation
↑ Plaque Formation (Athero)
↑Arterial Stiffness (Sclerosis)

The Double Whammy Hypothesis

- The changing hormone environment with the menopausal transition brings functional alterations that make the arteries more susceptible to damage
- Mid-life is a time of increasing risk factors for women.
- Double Whammy: the arteries are being exposed to higher levels of risk factors at the very time they are becoming more susceptible to damage because of functional alterations driven by the changing hormone environment.