Biology of Premenopausal Protection

Wrap-Up Session

Key Points

- Context is everything
- Biological versus epidemiological:
  - Mechanistic approaches
  - Probabilistic approaches

Biology

- Clear cut effects of hormones (i.e., estrogens) can be characterized in tissue and whole organisms
- Specific pathways and effects elucidated in
  - Brain
  - Bone: ANGELS
    - are there other angels? Are there devils (oxysterols)?
  - Liver
  - Adipose tissue
  - Immune system (B cells)

Biological Models

- In vitro tissue: work out cellular pathways
- Small animal
  - Extrapolate mechanisms in physiological setting
- Large animal
  - Explore applicability to humans (provide ‘proof of concept’ for interventions)
- Human ‘experiments of nature’
  - ‘Proof of concept’ for interventions

Epidemiology

- We’re fat!
- We’re getting fatter!
- Adipology: new science linking epi to bio approaches
- Correlation
- Development of risk models
- Forms another basis for testing of interventions

Epidemiological Approaches

- Forces emphasis on *context*:
  - Social order
  - Non-specific interactions with aging
  - Most ‘risk factors’ small, not 100% consistent
- Provides directive clues for biology and supports therapeutic investigation

Critical Linkages

- Put on your geriatric hat:
  - Think aging all the time
  - It's the backdrop, and it changes
- Collaborative, cross-cutting research:
  - Program Project, interactive projects

Critical Linkages

- Patient-oriented research:
  - Human is the animal of interest, one of few that experiences menopause
- Practical issues of applicability
  - How can the science be most efficiently applied?

Cross-Cutting Issues

- Is there a ‘critical window’ for ET or HT intervention for different conditions?
  - Cognition
  - Cardiovascular protection
  - Bone
  - Adiposity
  - Immune system

Cross-Cutting Issues

- How best to incorporate ***multiple interacting*** systems into models, especially when they are ***non-linear*** (e.g., cytokines, the HPA axis)?

Cross-Cutting Issues

- How best to evaluate effects of discontinuation/episodic versus continuous regimens and formulations?