Mercury Modulation of the Immune Response

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Hg is an anti-infectant

- Hg compounds used to treat infections
  - e.g. syphilis
- and combat infections
  - disinfectant or preservative
All Hg is immunotoxic

- Hg\(^0\), iHg, MeHg, EtHg – all effect immune system
  - Cellular (\textit{in vitro})
  - Experimental (\textit{in vivo} animal models)
  - Epidemiological
Lack of concordance

• Interactions between Hg and risk/susceptibility factors
  – Neurotoxicity, including at low exposures
    Evidenced in individuals co-exposed to Hg and infection
  – Increased autoimmune response
    Evidenced in individuals co-exposed to Hg and “trigger”, eg. CVB3
  – Suppression of primary immune response
    Evidenced in individuals co-exposed to Hg and infection, eg. malaria
Mouse model of autoimmune heart disease

- CVB3 virus-induced model (BALB/c)

![Graph showing viral and autoimmune phase]

- Viral phase
- Autoimmune phase

Hg dosing:
- pretreatment
- interim treatment

- virus infection (day 0)
- harvest (day 12)
- harvest (day 35)
Hg modulates the autoimmune disease


**A. Myocarditis Hg Pretreatment**

- **% inflammation**
  - Viral: Hg alone > PBS > Hg
  - Autoimmune: Hg alone > PBS > Hg

**B. Virus Titer Hg Pretreatment**

- **PFU/g heart**
  - Viral: Hg alone > PBS > Hg
  - Autoimmune: Hg alone > PBS > Hg

Dilated cardiomyopathy

No virus reactivation

PBS

Hg

Hg increases fibrosis in the heart

Hg interacts with viral trigger

- Increased macrophage infiltration

Hg induces autoimmune dysfunction

- Timing of environmental exposure is critical
- Modulation of innate immune cells (macrophages) – shifting phenotype
- Changes the milieu at the point of infection
- Increases inflammation and disease
Why the inconsistencies?

• What’s different in various studies?
  – Exposure levels
  – Species of Hg
  – Co-exposures: infection, xenobiotics, medicine
  – Genetic background: sex and other risk factors

• Hg may be necessary but not sufficient to induce immune-related adverse outcomes
Where do we go next?

• epigenetics?
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