

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

- Hg⁰, iHg, MeHg, EtHg – all effect immune system
 - Cellular (*in vitro*)
 - Experimental (*in vivo* animal models)
 - Epidemiological

Lack of concordance

- Interactions between Hg and risk/susceptibility factors
 - Neurotoxicity, including at low exposures

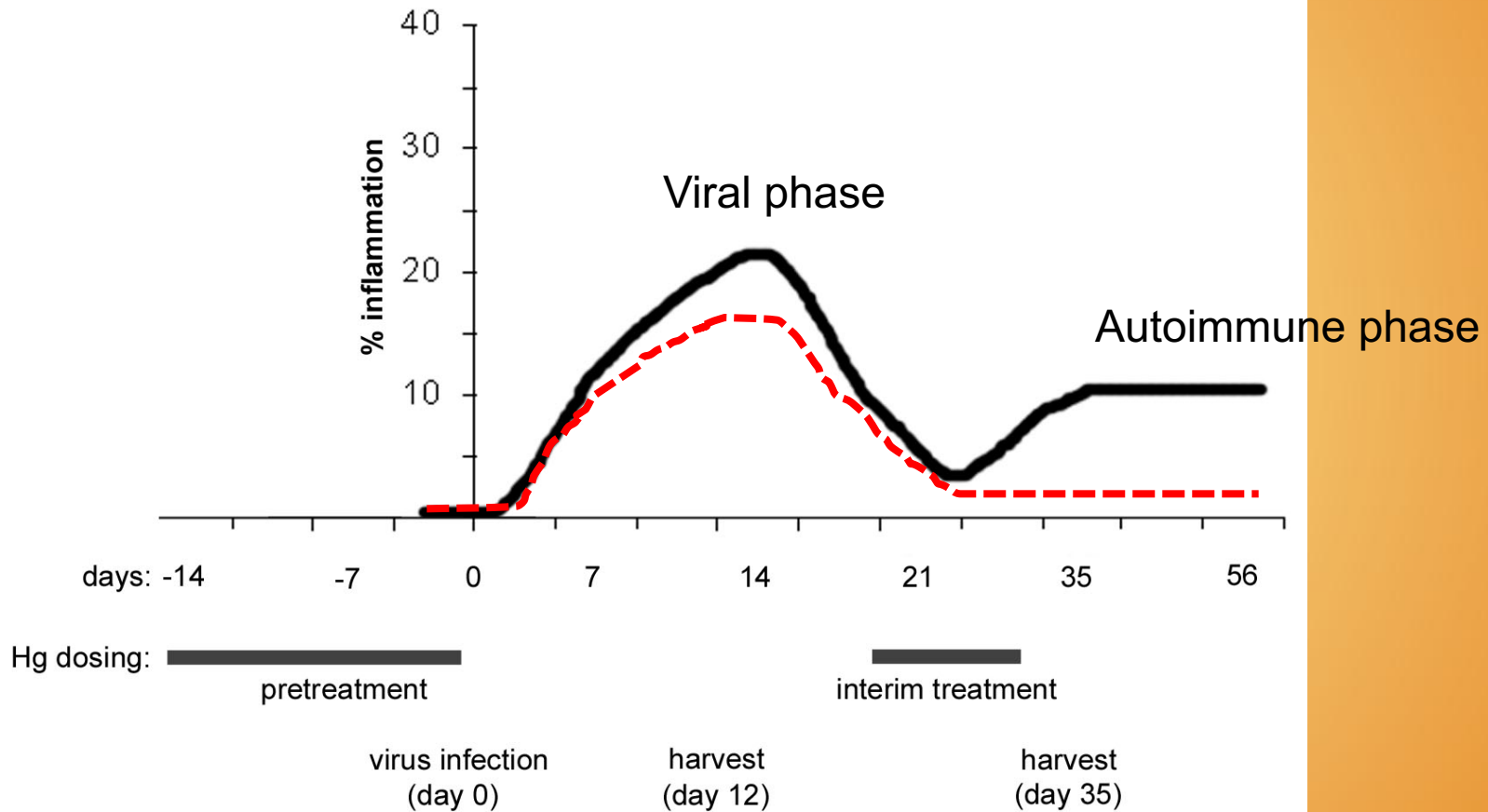
Evidenced in individuals co-exposed to Hg and infection
 - Increased autoimmune response

Evidenced in individuals co-exposed to Hg and “trigger”, eg. CVB3
 - Suppression of primary immune response

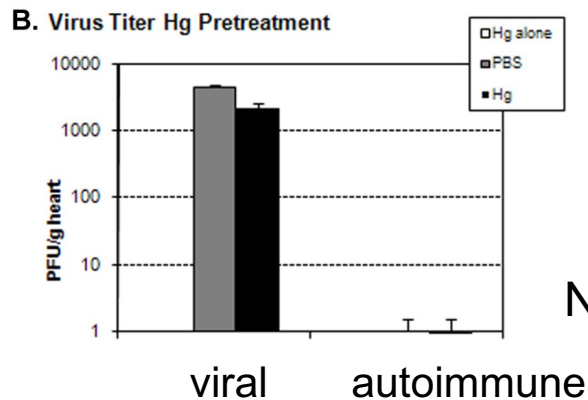
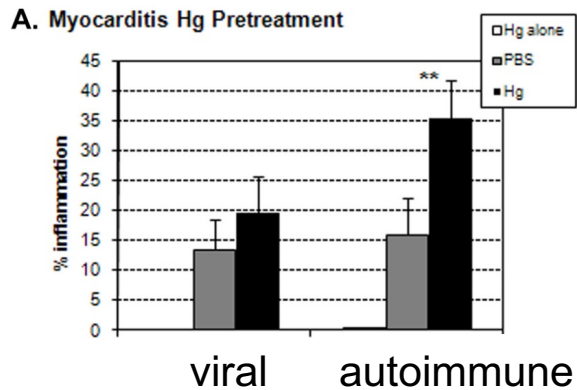
Evidenced in individuals co-exposed to Hg and infection, eg. malaria

Mouse model of autoimmune heart disease

- CVB3 virus-induced model (BALB/c)



Hg modulates the autoimmune disease



Dilated cardiomyopathy

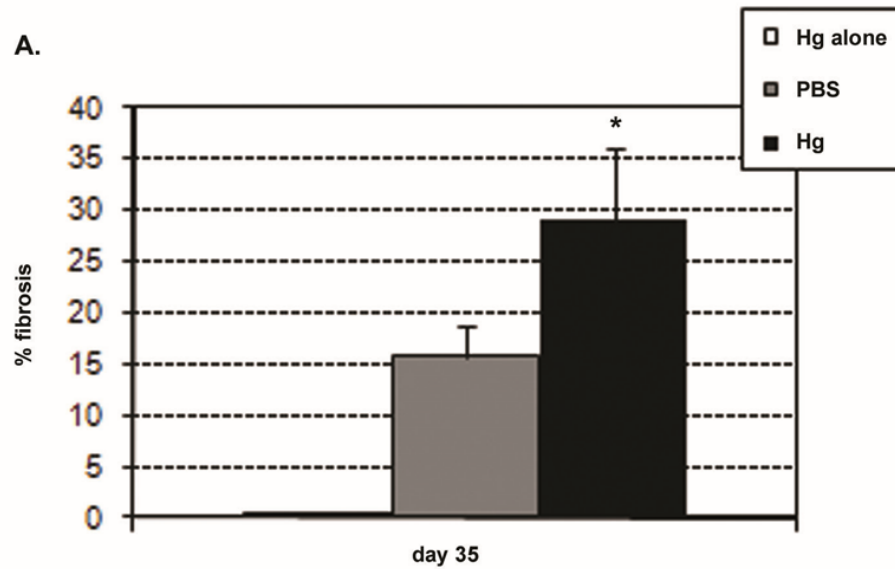


PBS

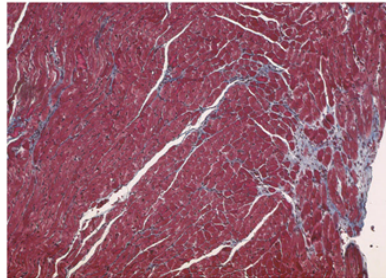
Hg

No virus reactivation

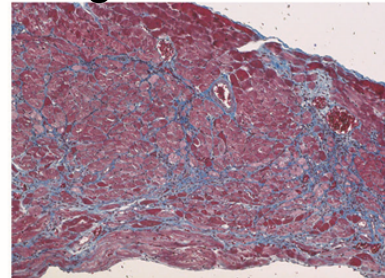
Hg increases fibrosis in the heart



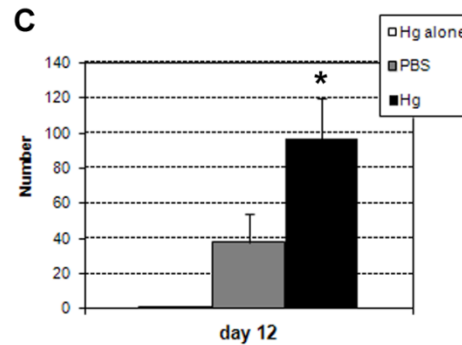
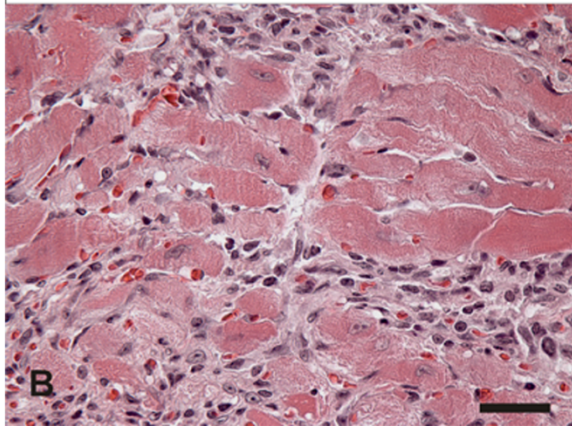
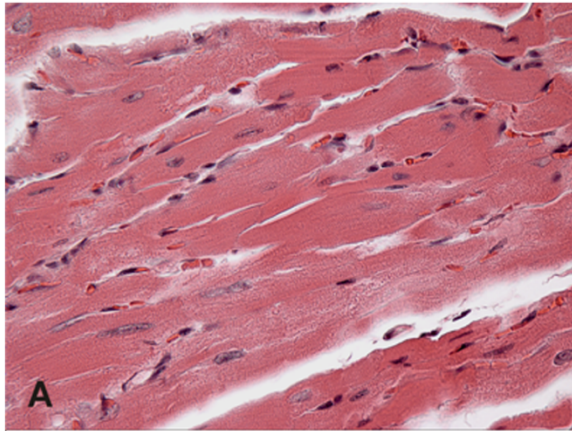
B. PBS



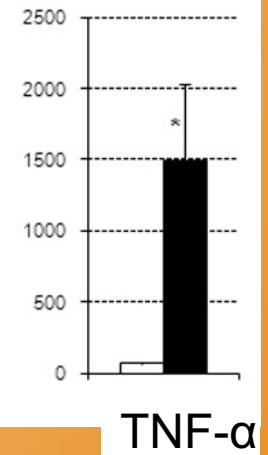
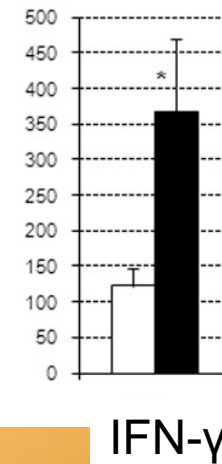
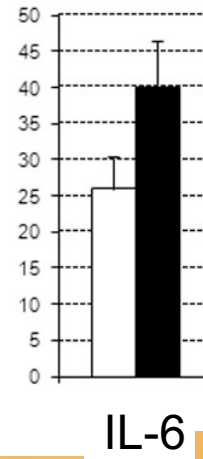
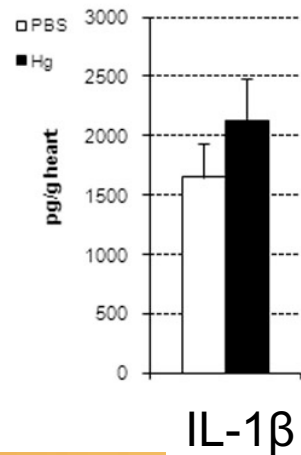
c. Hg



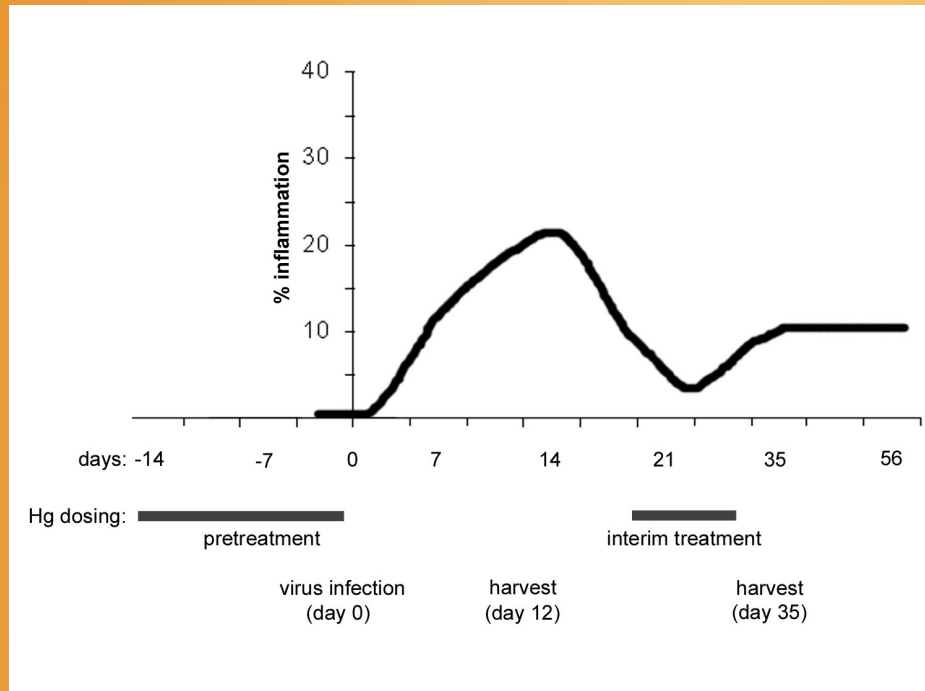
Hg interacts with viral trigger



- 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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